THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

Vol. 55 FEBRUARY, 1946 No. 2

LIPOMA OF THE CORPUS CALLOSUM*

A CLINICOPATHOLOGIC STUDY

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THE corpus callosum appears to be one of the favorite sites of cerebral lipoma. The world's literature contains 30† cases involving the corpus callosum among a total of approximately 100 known examples of lipoma of the brain.

Most publications on cerebral lipoma have appeared in the European literature and the excellent paper by Krainer[1] (1935) is especially recommended. Practically all authors have limited their study to the pathologic and anatomic aspects of the problem and have advanced various theories as to the pathogenesis of cerebral lipoma.

The purposes of this contribution are (1) to survey the extensive literature on lipoma of the corpus callosum, (2) to describe its anatomic aspects and (3) to discuss certain roentgenologic features which may permit one to make the diagnosis of lipoma of the corpus callosum *intra vitam*.

A tabulation of all previously recorded cases is included (Table 1) and 2 additional cases are reported in full to illustrate the salient points of the problem.

CASE REPORTS

CASE 1. J.M. (No. 551516), male, aged forty-four, was admitted to the University Hospital on July 13, 1944, referred by Dr. J. Grekin, of Detroit. For the past two years the patient had suffered from frequent headaches and convulsive attacks. These seizures usually had been of left motor jacksonian type, but occasionally right-sided convulsions had also occurred. The attacks were frequently followed by headache, vomiting, and mental confusion. A few weeks prior to admission, a mild left hemiparesis had gradually developed.

On examination, the patient exhibited a mild organic brain syndrome with memory loss, intellectual and affective dulling, and tendency to perseveration. The ocular fundi were normal. Except for a left lower facial paresis on emotional innervation, cranial nerve function was not disturbed. There was a mild left spastic hemiparesis, being most noticeable in the left leg; also the right lower extremity showed slight increase of muscle tone. Diadochokinesis was slowed in the left hand. Deep reflexes were exaggerated throughout, particularly in the left upper and right lower extremity. The right abdominal reflexes were absent, the left ones diminished. Rossolimo's sign was present bilaterally, but Babinski's sign was

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† This includes the two observations presented in this paper.

TABLE I

REPORTED CASES OF LIPOMA OF CORPUS CALLOSUM

Number	Year	Author	Age	Sex	Anatomical Findings	Clinical Findings
1	1856	Rokitansky[2]	26	F	Pea sized, on posterior part of corpus callosum	None
2	1856	Rokitansky[2]	5	M	Cylindric lipoma	None
3	1858	Benjamin[3]	32	F	Cylindric lipoma with calcification and ossification; corpus callosum atrophic	Hemiparesis, convulsions
4	1863	Virchow[4]	20	F	Fat strip on raphe	
5	1863	Virchow[4]			Along fornix	
6	1869	Parrot[5]	2	F	Flat lipoma	None
7	1873	Chouppe[6]	45	F	Multiple lipomas, one on each side of raphe, a third between olfactory bulb and midline	Headaches, vomiting, hemiparesis, convulsions, mental changes
8	1874	Coats[7]	38	F	Flat lipoma	None
9	1887	Leichtenstern[8]			Flat lipoma	None
10	1895	Pugliese[9]	31	M	Flat lipoma	Mental changes
11	1897	Bostroem[10]	39	F	Lipoma of genu	None
12	1902	Della Rovere[11]	43	F	Streak-like	None
13	1902	Würth[12]	14	F	Large ovoid lipoma; corpus callosum and left cerebral hemisphere atrophic; calcification present	Mental deficiency, convulsions, hemiparesis
14	1902	de Steiger[13]	37	F	Lipoma of entire corpus callosum; separate nodule in choroid plexus; calcification	Mental changes
15	1903	Kirkbride[14]	54	M	Flat lipoma, connected with choroid, plexus; corpus callosum hypoplastic	None
16	1904	Bartel[15]	15	F	Flat lipoma; 2 nodules in choroid plexus	
17	1905	Ernst[16]	53	M	Flat lipoma with ossification; corpus callosum hypoplastic	None
18	1907	v. Sury[17]	66	F	Cap-like lipoma with calcification; corpus callosum hypoplastic	
19	1910	Abrikossow[18]	3	M	Lipoma of corpus callosum; two nodules in choroid plexus	
20	1920	Körner[19]	44	F	(Quoted by Krainer) no data available	
21	1921	Huebschmann[20]	3	M	Lipoma of genu; posterior half of corpus callosum absent	Mental deficiency, convulsions
22	1928	Huddleson[21]	46	M	Walnut-sized lipoma on genu with calcification; absence of corpus callosum and septum pellucidum	None
23	1932	Rubinstein[22]	30	F	Flat lipoma with calcification; separate nodules on choroid plexus; partial agenesis of corpus callosum and fornix	Mental deficiency, convulsions
24	1936	Juba[23]			Flat lipoma with partial agenesis of corpus callosum	
25	1938	Gander[24]	29	M	Fat strip on each side of raphe	None
26	1938	Fattovich[25]	75	F	Flat lipoma over entire length of corpus callosum	Senile psychosis, probably unrelated
27	1945	Ehni and Adson[26]	18	F	Ovoid lipoma at anterior part of corpus callosum; partial agenesis of corpus callosum	Convulsions; calcification visible on roentgenogram. Operated on as brain tumor. Autopsy

Table I—*Continued*

Number	Year	Author	Age	Sex	Anatomical Findings	Clinical Findings
28	1945	Ehni and Adson[26]	16	F	Posterior part of corpus callosum	
29	1945	List, Holt and Everett, Case 1	44	M	Ovoid lipoma in region of genu; posterior part of corpus callosum absent; calcification	Headaches, convulsions, hemiparesis. Lipoma surgically removed. Died 5 months later. No autopsy
30	1945	List, Holt and Everett, Case 11	3 days	F	Cap-like, covering entire length of hypoplastic corpus callosum; separate nodules in choroid plexus; calcification in adjacent brain tissue; septum pellucidum absent; malformed cortical convolutions; lumbosacral myelomeningocele; subependymal heterotopias of gray matter in lateral ventricles	Ruptured lumbosacral myelomeningocele with paralysis of lower extremities; hydrocephalus

negative. No sensory changes were elicited. The gait was mildly hemiparetic on the left.

Electroencephalography revealed a generalized epileptoid pattern with occasional bilateral discharges from the anterior temporal regions. This was interpreted as an indication of a deep lesion in the forebrain.

Roentgenograms of the skull showed persistence of the frontal (metopic) suture and absence of the frontal sinuses. Sagittal projections disclosed two crescentic calcium deposits surrounding the midline in the posterior frontal region (Fig. 1). The calcium deposits could not be identified in lateral views, but here an ovoid zone of decreased density occupied the midportion of the posterior frontal area (Fig. 2).

Fig. 1. Case 1. Roentgenogram of skull in frontal projection showing two crescentic lines of calcification outlining the lipoma. Note persistence of midfrontal suture and undeveloped frontal sinuses.

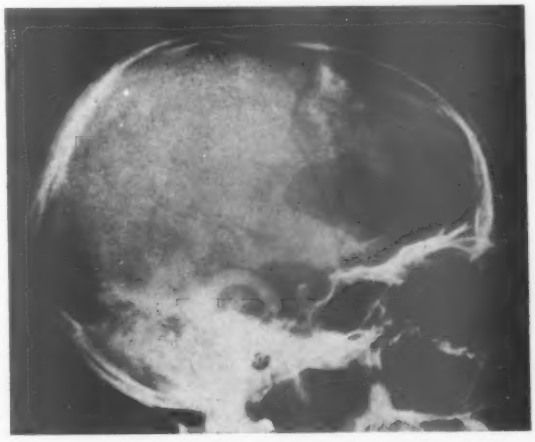

Fig. 2. Case 1. Roentgenogram of skull in lateral projection. Area of increased radiolucency in midfrontal region indicates lipoma (retouched).

Ventriculograms suggested that the anterior portions of the lateral ventricles were spread by a midline mass, the periphery of which was partially outlined by the calcification described above. The posterior portions of the lateral ventricles were moderately dilated and the

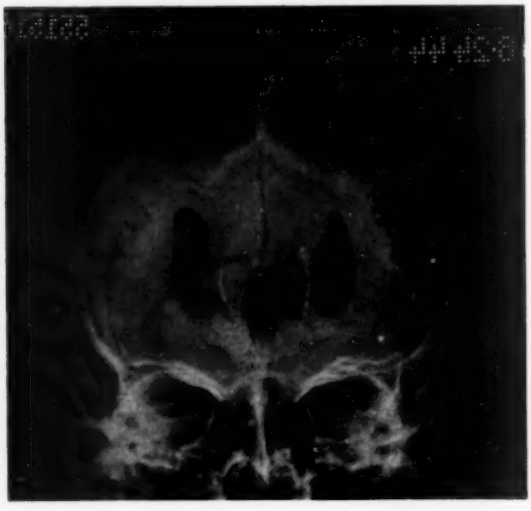

FIG. 3. Case 1. Ventriculogram in frontal projection showing the frontal horns of lateral ventricles separated by lipoma. The dilated third ventricle appears elevated due to agenesis of the corpus callosum (slightly retouched).

slightly enlarged third ventricle was displaced upwards (Fig. 3).

The diagnosis was made of a partially calcified tumor in the frontal midline area, associated with agenesis of the corpus callosum. A congenital lesion such as a lipoma, dermoid or complex teratoma was suspected. Exploration was decided upon because the patient's symptoms were progressive.

Operation was performed on August 25, 1944. Avertin-intratracheal ether anesthesia was used. A large right frontal osteoplastic flap was turned, crossing the midline to obtain adequate access to the region of the corpus callosum. After coagulation and sectioning of several veins connecting the frontal lobe with the superior sagittal sinus, and, after splitting of the falx, the midline structures could be clearly exposed. The posterior part of the corpus callosum was absent and instead, there was an opening leading into the lateral ventricles, covered only by arachnoid. The anterior part of the corpus callosum was replaced by an ovoid, encapsulated yellow tumor, the size of a large plum. It had the gross appearance of a lipoma. Demarcation from the frontal lobes was sharp. Both of the rather large anterior cerebral arteries and their branches were incorporated in the tumor capsule. The attempt to dissect the tumor *in toto* had to be abandoned because both anterior cerebral arteries deeply penetrated the growth. In an endeavor to save these vessels, the tumor was removed piecemeal, yet eventually it became necessary to clip the right anterior cerebral artery and also some branches of the left. After the inner core had been excavated, the firm capsule with its areas of calcification was removed from both frontal lobes. Following complete extirpation, it was realized that the tumor had replaced the knee of the corpus callosum and septum pellucidum, extending basally to the supraoptic area and posteriorly into the frontal horns of both lateral ventricles. After carefully establishing hemostasis, dura, pericranium, galea, and scalp were closed in layers with silk sutures.

Histopathologic examination proved the removed tissue to be a mature, encapsulated lipoma, containing many arteries and veins. Scattered calcium deposits resembling psammoma bodies were present in the adjacent brain and also in the connective tissue strands of the lipoma (Fig. 4).

The postoperative course was grave. For the first four days, the patient was comatose. His rectal temperature fluctuated between 102 and

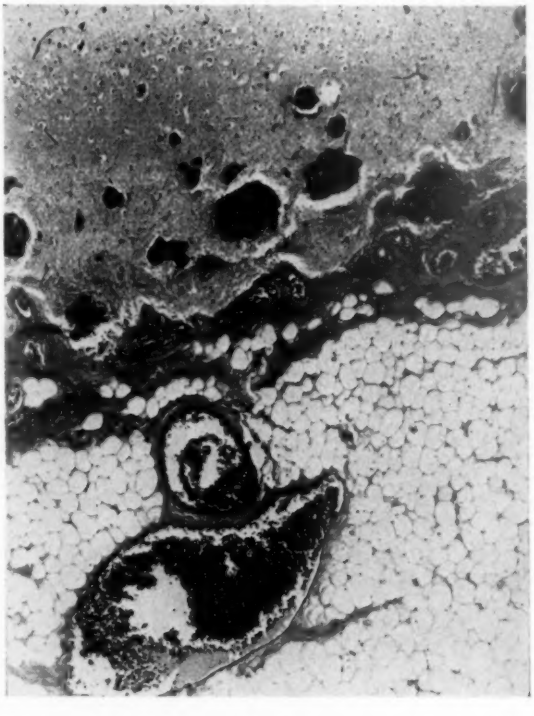

FIG. 4. Case 1. Histopathologic picture of operative specimen showing mature lipoma with large blood vessels, pial capsule and areas of calcification in the adjacent brain tissue.

104°F., respirations between 36 and 44, and he hiccuped frequently. When consciousness began to return on the fifth postoperative day, complete right hemiplegia and paresis of the left leg were noted. It was assumed that, due to the surgical manipulation, thrombosis of both anterior cerebral arteries had occurred with resulting extensive softening, especially of the left cerebral hemisphere, and damage to the hypothalamus. In the course of several weeks, however, a gradual improvement took place and the temperature became normal.

On discharge six weeks after operation, the patient presented a profound organic brain syndrome with generalized psychomotor akinesis. Speech was monosyllabic and reiterative. A right-sided pyramidal-extrapyramidal hemiparesis was present, especially in the lower extremity, and also a slight paresis of the left leg. Bilateral forced grasping was noted. The patient was incontinent of urine. He could walk by himself, but with a bilateral spastic "marche à petit pas."

Three months later, he began to deteriorate gradually, both mentally and physically, and developed fever. He was then admitted to another hospital where he showed signs of progressive cerebral thrombosis or possibly late intracerebral infection. He died there, five months after the original operation. Unfortunately autopsy was not obtained.

Case II. A female infant (No. 514642), aged thirty-six hours, was brought to the University Hospital on October 26, 1942, because of myelomeningocele. She had been delivered by cesarean section at another hospital. Examination revealed slight enlargement of the head (14 inches in circumference) with widely open fontanelles. There was a large lumbar myelomeningocele which had perforated spontaneously and drained spinal fluid. Both lower extremities were flaccid and completely paralyzed.

The infant was in poor condition throughout her stay in the hospital and she died on the third day. Permission for autopsy was obtained.

Autopsy. The pathological changes were found to be confined to the nervous system. There was a ruptured myelomeningocele (2.25 by 5 cm.) extending from the lumbar area to the sacrum, with acute purulent inflammation at its upper pole.

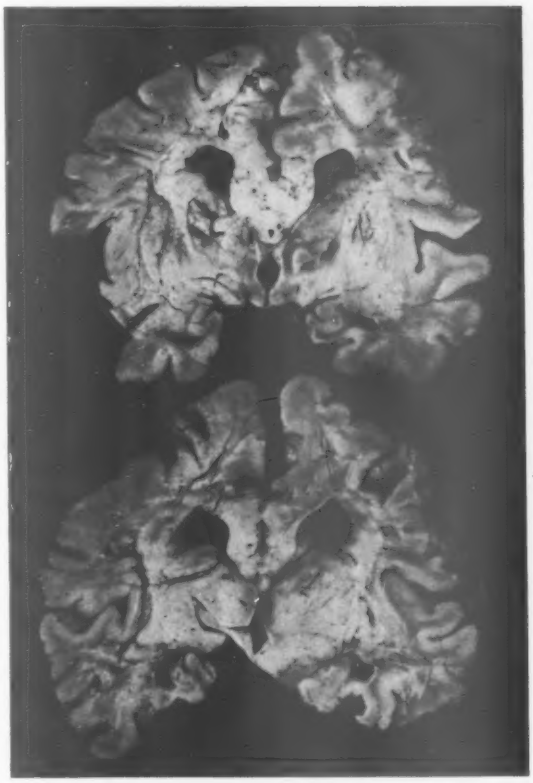

Fig. 5. Case II. Coronal sections of the brain showing the lipoma of the corpus callosum.

Examination of the brain showed the convolutions to be small and malformed. In coronal sections, the cortex was thinned and the lateral ventricles moderately dilated. The corpus callosum was replaced by a yellowish gray mass, measuring 2 by 2.25 cm. in the region of the genu and tapering posteriorly to 1.25 by 1.25 cm. in the splenial region (Fig. 5). The septum pellucidum was absent.

The fornix appeared to be incorporated in the tumor. Gray, pea-sized nodules were seen beneath the ependyma of the posterior horns of the lateral ventricles. All other parts of the brain and the rest of the body were essentially normal.

Microscopic Examination. There was acute purulent inflammation of the spinal cord and subcutaneous tissues at the site of the myelomeningocele. The cell layers of the cerebral cortex were poorly developed and the convolutions malformed. The subependymal nodules of the cerebral ventricles proved to be heterotopic islands of gray matter. The corpus callosum consisted of only a few thin strands

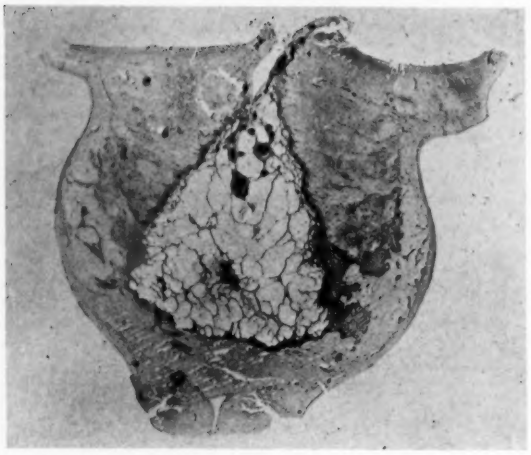

FIG. 6. Case II. Stained coronal section through callosal region at low magnification showing the relation of central lipoma to the underlying hypoplastic corpus callosum.

crossing in the region of the genu and splenium. The remainder was replaced by a vascular lipoma made up of fat cells of adult type (Fig. 6). Two rather large vessels, apparently the anterior cerebral arteries, passed directly through the center of the tumor. There were areas of calcification in adjacent brain tissue. The cerebellum was poorly developed. The fornix, basilar ganglia, and medulla were normal.

I. ANATOMIC CONSIDERATIONS

A. Macroscopic Anatomy. A lipoma of the corpus callosum is always situated on its dorsal surface and closely follows the contours of that structure. Most frequently, the tumor occupies the anterior part of the corpus callosum; less often it covers the entire length, or shows its greatest development in the splenial region. Since the lipoma is located beneath the leptomeninges, the arachnoid or pia of the sulcus corporis callosi forms what appears to be the capsule of the lipoma. Consequently, both anterior cerebral arteries are incorporated in the growth or its arachnoidal covering, sending many branches into the interior. The lipoma forms either an ovoid mass or a thin, streak-like layer; in some instances, it consists of two longitudinal columns with a central groove, corresponding to the median raphe. Anteriorly located lipomas may extend to the lamina terminalis and involve the septum pellucidum and fornix.

There is considerable variation in size, the largest callosal lipomas observed attaining nearly the size of a hen's egg; the smallest, that of a pea. Occasionally, additional separate small lipomatous nodules were observed in the plexus choroideus (Rubinstein,[22] Abrikossow,[18] Bartel,[15] de Steiger,[13] our Case II) or in the region of the olfactory nerve (Chouppe).[6]

Most lipomas of the corpus callosum are perfectly demarcated from adjacent structures of the brain. In rare instances (Huddleson),[21] they may give the appearance of infiltration into cerebral tissue. Calcification or even ossification occurs frequently (cases of Benjamin,[3] v. Sury,[17] de Steiger,[13] Ernst,[16] Rubinstein,[22] Huddleson,[21] Würth,[12] Ehni and Adson,[26] our cases). The calcium deposits may be macroscopically visible. They are found mainly in the peripheral portions of the tumor, its capsule or adjacent cerebral tissue. In Benjamin's[3] exceptional case, the entire central core of the lipoma consisted of an osseous mass.

B. Histopathologic Structure. The microscopic picture of cerebral lipoma does not differ from typical mature lipoma or fibrolipoma found in other parts of the body. Histopathologic evidence of malignancy, such as infiltration, excessive mitoses, or atypical cells are absent. The occasional presence of young mesenchymal cells in the peripheral zone or capsule (Huddleson)[21] does not necessarily mean active infiltrative proliferation, but may be a secondary reparative reaction of the damaged surrounding brain tissue.*

Cerebral lipomas never contain neural elements except those which originate from the neighboring brain and become accidentally included. It is also worthy of mention that dermal structures or cutaneous appendages never have been observed in cerebral lipomas. Calcium deposits may occur in the lipoma and adjacent brain as amorphous concrements,

* Analogous changes are found in the marginal zone of meningiomas.

as concentrically arranged bodies resembling psammoma bodies, or as islands of true bone. This calcification is generally interpreted as evidence of retrogressive change.

C. Associated Anomalies. Lipoma of the corpus callosum is often combined with other developmental anomalies of both the central nervous and skeletal systems. It is not surprising to find the lipoma associated with a defect of the corpus callosum. Total absence of this structure was observed by Würth,[12] Huddleson[21] and by us (Case I); partial agenesis was noted by Benjamin,[3] v. Sury,[17] Juba,[23] Huebschmann,[20] Rubinstein,[22] Ehni and Adson,[26] and by us (Case II). In Huddleson's case and our observations, the septum pellucidum was also absent, and in Rubinstein's case the fornix was hypoplastic. The question arises whether the defect of the corpus callosum is primary and leads to a compensatory formation of fatty tissue, or whether agenesis of the corpus callosum is secondary to the presence of the lipoma. Most evidence favors the latter view, *viz.*, that the lipoma develops at a very early embryonic period and interferes with the formation of the interhemispheral commissural system during the third and fourth fetal months. The callosal fibers then become deflected and instead of following their normal transverse direction, form a longitudinal fascicle (so-called "Balkenlängsbündel" of German authors). Since the corpus callosum develops in an anteroposterior direction, the presence of a lipoma inhibits formation of its posterior portion.

Other associated abnormalities of the brain have been found, such as atrophy of one hemisphere (Würth)[12] and malformation of the cortex (our Case II).

It seems to us of significance that the skeletal deformities occasionally associated with lipoma of the corpus callosum belong to the so-called dysraphic state. In our first case, there was persistence of the mid-frontal suture; in the second case, lumbosacral spina bifida and myelomeningocele were present. Huebschmann's[20] patient had a funnel chest. A most unusual observation of Arnold[27] may be mentioned here, because it illustrates the combination of lipoma, dysraphic disorder and agenesis of corpus callosum in a nine-month-old boy: A large extracranial lipoma of the frontal region extended through the anterior fontanelle and gaping mid-frontal suture, and through a dural opening, into the cranial cavity. The tumor continued between both frontal lobes into the ventricular space. Corpus callosum, septum pellucidum and fornix were present.

D. Pathogenesis. Various theories concerning the morphogenesis of cerebral lipoma will now be reviewed in the light of available anatomic and embryologic evidence. It had been assumed that cerebral lipoma might develop by hypertrophy from pre-existing fatty tissue of the meninges (Virchow),[4] or possibly by transformation or metaplasia of meningeal connective tissue (Pugliese),[9] but these theories are now considered as untenable.

Recognizing its dysontogenetic character, Bostroem[10] grouped cerebral lipoma with intracranial dermoid and epidermoid. He regarded all these lesions as heterotopic malformations of dermal origin and assumed that either the ectodermal elements of the original dermal anlage had disappeared, thus leaving a residual lipoma, or that only a few cells of the dermal anlage, with potentiality of differentiating into a lipoma, were displaced. Bostroem's hypothesis explains well the predilection of cerebral lipoma for midline structures, but it fails to account for the complete absence of dermal elements in these growths.

Verga[28] and Krainer[1], whose theory appears to be most acceptable to us, considered cerebral lipoma as a tumor-like malformation, derived from the primitive meninx. Krainer stated that, as a rule, the lipoma occurs in the leptomeningeal cisterns (e.g., the cisterna corporis callosi) and in the tela choreoidea. He also emphasized the fact that the lipoma respects meningeal and neural structures and thus behaves like a malformation rather than a true neoplasm. If there is maldifferentiation or persistence of the primitive mesenchymal

reticulum surrounding the meningeal vessels, a lipoma may develop instead of the normal, fluid-containing leptomeninges. This concept agrees well with Wassermann's[29] fundamental work on the development of adipose tissue. According to this author, mature fatty tissue is derived from primitive perivascular reticulo-endothelium which, instead of subserving hematopoietic function, becomes specialized in the storage of fat. Since the perivascular reticulo-endothelium is ubiquitous and thus present in the primitive meninx, the formation of a pial lipoma can be easily explained. On the other hand, the rarity of cerebral lipoma and its selective location suggests the presence of additional local factors which are probably determined by developmental faults of the nervous system. Ehni and Adson[26] attributed the formation of lipomas (especially those of the spinal cord) to developmental disturbances of the neural crest. The frequent occurrence of cerebral lipoma in or close to the midline may be explained by a disturbed closure of the neuraxis in the posterior midline, associated with maldifferentiation of the primitive meninx. In other words, a dysraphic disorder is often an associated, if not predisposing factor for the formation of a lipoma.

II. CLINICAL CONSIDERATIONS

A. Incidence. Cerebral lipoma has no preference for sex or age. Its occurrence in early childhood is further evidence of its dysembryonic character. That lipoma has been incidentally encountered at autopsy in very old persons proves that it does not possess the active growth tendency of true neoplasms.

B. Clinical Symptomatology. Little is known about the clinical symptomatology of lipoma of the corpus callosum. The scarcity or even total absence of clinical symptoms and signs is not surprising, considering the small size of some of these lesions, their congenital origin, and lack of expansive growth. On the other hand, they may interfere with the circulation in both anterior cerebral arteries and thus cause clinical symptoms. In some patients (Benjamin,[3] Chouppe,[6] Würth,[12] Huebschmann,[20] Rubinstein,[22] Ehni and Adson,[26] and our own), mental changes, convulsive attacks and hemiparetic signs were reported. In our Case 1, motor jacksonian attacks with bilateral mild hemiparetic manifestations presented suggestive evidence of a parasagittal, possibly callosal, lesion with involvement of both frontal lobes. The syndrome was not clear cut, however, and did not correspond to the symptom complex of a vascular lesion of the anterior cerebral arteries. Signs of increased intracranial pressure reported by Chouppe[6] are, as a rule, absent, even though the lipoma is of sizable proportions.

It is certainly impossible to diagnose lipoma of the corpus callosum from clinical evidence alone, and its uncharacteristic symptomatology permits no clinical differentiation from cases of agenesis of the corpus callosum. It is therefore, fortunate that certain roentgenologic features of these lesions are so highly characteristic that in some instances, at least, a definite diagnosis during life is possible.

C. Roentgenologic Aspects. So far as we have been able to determine, the recent publication of Ehni and Adson[26] is the only one mentioning roentgenologic signs associated with lipoma of the corpus callosum. Sosman[30] presented the findings in 4 patients in whom he had made the diagnosis of such abnormality, but as yet his report has not appeared in print.*

Because the roentgen-ray coefficient of fat is appreciably less than that of any other body tissue, fat will be represented in the roentgenogram as a zone of increased radiolucency. In the case of a sizable intracranial lipoma, the tumor will reflect itself as a well demarcated area of decreased density standing out clearly against the denser background of the cranial vault. Ehni and Adson[26] did not mention this

* Sosman also described the roentgen signs of callosal lipoma in the discussion of a paper entitled "Midline Anomalies of the Brain" by A. P. Echternacht and J. A. Campbell. This paper was presented at the Joint Meeting of the American Roentgen Ray Society and the Radiological Society of North America in Chicago, Ill., Sept., 1944. (*Radiology*, Feb., 1946, *46*, 119-131.)

feature although it appears to be present in reproductions of roentgenograms used to illustrate their article.

Calcification or ossification of a lipoma may partially or entirely obscure the characteristic radiolucency of the fat cells, but if this calcium deposit outlines the smoothly rounded periphery of the tumor, it furnishes another clue to the type of lesion present. In one of our patients (Case 1), the crescentic outer margins of the calcified tumor capsule were clearly discernible in sagittal projections of the skull, but no central zone of decreased density due to the presence of fat was evident (Fig. 1). In lateral projections of the same skull, however, the calcium deposits were too thin to be recognizable and the lesion was represented by a zone of increased radiolucency. Admittedly, this feature was seen only in retrospect (Fig. 2).

As previously stated, intracranial lipoma commonly arises in the anterior portion of the corpus callosum and is frequently associated with agenesis of the posterior portion of that structure, another condition in which diagnosis during life is possible only by employment of roentgenologic methods. Davidoff and Dyke[31] were the first to describe the characteristic encephalographic findings in agenesis of the corpus callosum and they especially emphasized the concavity of the mesial margins of the widely separated lateral ventricles as an important diagnostic sign. This feature is even more pronounced when an associated space-occupying lipoma is present (Fig. 3). One should not assume that these two lesions are always coexistent. Only a minority of the verified cases of lipoma showed agenesis of the corpus callosum. Bunts and Chaffee[32] reviewed 15 cases of agenesis of the corpus callosum discovered by roentgenographic means. The diagnosis was confirmed by craniotomy in at least 5 of these patients, but no reference was made to the presence of an associated lipoma in any of them.*

To recognize the roentgen signs of lipoma of the corpus callosum, one must be constantly on guard to identify intracranial calcification and, more importantly, to prevent mistaking the pathognomonic zone of radiolucency for an area of bone erosion or even a fortuitous overlapping of prominent digital markings in the cranial vault. Since the density of air and of fat is almost identical, pneumoencephalography, so essential in the diagnosis of associated agenesis of the corpus callosum, is indicated only after plain skull roentgenograms have been obtained.

D. Neurosurgical Aspects. It is evident that lipoma of the corpus callosum is seldom, if ever, amenable to neurosurgical treatment, and only 2 cases of surgical removal are on record (Ehni and Adson,[26] and our Case 1). Although the excision of an ovoid or globular lipoma is technically possible, the crux of the situation lies in the fact that both anterior cerebral arteries are firmly embedded in the capsule or in the anterior of the tumor. Injury to these vessels is almost unavoidable when extirpation of the lesion is attempted. The resultant grave disturbances due to ligation or thrombosis of these vessels are well demonstrated by the postoperative course both in Ehni and Adson's patient and our Case 1. Ehni and Adson's patient died a few days after operation. In our own observation, the postoperative sequelae reduced the patient to a hopeless "brain cripple" and eventually led to his death five months later. The operation was undertaken because no accurate diagnosis was made as to type of tumor, and the important relationship of the anterior cerebral arteries to the tumor was not clearly realized preoperatively. We wish to state, therefore, that surgery is contraindicated if the diagnosis of lipoma of the corpus callosum can be made preoperatively.

SUMMARY

The literature on lipoma of the corpus callosum is surveyed and two case reports are added.

The anatomic features of these lesions

* One of our own observations of callosal agenesis was surgically verified but no lipoma was present.

are described and their pathogenesis discussed.

Even though the clinical symptomatology is not pathognomonic, the diagnosis of lipoma of the corpus callosum can occasionally be made during life by roentgenographic means. The roentgenographic signs consist of increased radiolucency of the tumor, calcification, demonstration of an expanding mass in the anterior part of the corpus callosum and agenesis of the posterior portion of this structure.

Surgical treatment of lipoma of the corpus callosum is contraindicated.

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NEWER INVESTIGATIONS OF RADIATION EFFECTS AND THEIR CLINICAL APPLICATIONS

PANCOAST LECTURE*

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INTRODUCTION

IT IS with a great deal of pleasure that I accept the honor of giving the Pancoast Lecture, because I doubt if any man had a higher regard for the personal or masterly qualities of mind and a greater capacity for friendship than Dr. Pancoast exhibited.

If it be true that we stand on the shoulders of those who have preceded us, certainly we who practice radiology should have a far vision, having stood upon the broad shoulders of Henry Pancoast. Not only was he large in stature but also in the breadth of his vision and the application of his active mind toward the solution of many of the problems which daily confront the radiologist. He exhibited a fine discrimination between merit and pretense, as shown by the type and quality of young men with whom he surrounded himself. He was a particular friend of the younger men in radiology and at any of the annual meetings one would see him in the center of such a group who were eagerly asking questions and receiving helpful answers. He was a man not given to flattery, and he accepted it with ill grace, and I am sure that if he were here this evening he would care much less for the plaudits bestowed upon him than for the subject of the discussion. He was interested in the larger aspects of radiology, as well as its minutiae, and it is with the latter that we are concerned in the topic for this evening, namely, "Newer Investigations of Radiation Effects and Their Clinical Applications."

When one speaks of "newer investigations of radiation" today, it is usually safe to assume that he means the amazing developments of modern nuclear physics and artificial radioactivity. It is well to remember, however, that this is only one branch of atomic physics, and that another branch leading to advancement in radiation therapy has been progressing rapidly. In addition to fundamental physics, the advancements in technology today have put into our hands the means of understanding and making use of for the first time facts that may have been known in an inexact way for many years, as well as the means for gaining new facts. At the same time, there have been great advances in chemistry and physiology, without which the new fundamental knowledge of physics could not be integrated into an advance in medicine. Thus, as always, if science progresses at all, it progresses not in individual pieces, but as an integrated whole.

The age of advancement in the field of radiation therapy, which had its beginnings in the labors of Pfahler, Pancoast and other scientists, is therefore far from ended. Today, the radiologist is more than ever able to take all of the related researches from the fields of physics, chemistry and physiology, to correlate them, and to use them to build further knowledge on the foundation laid by these men.

When a patient is treated with a beam of radiant energy, nothing will happen unless some part of that energy is absorbed. It will be absorbed in part by both the normal structures of the body and by the disease process under treatment. The mechanism of the resulting reaction constituted an intriguing problem from the earliest days of radiation therapy, but curiously enough not until 1922 was there a worth while theory advanced for its

* The Pancoast Memorial Lecture, presented before the Philadelphia Roentgen Ray Society, November 5, 1942.

explanation. In that year, Dessauer published his "point heat hypothesis" according to which absorption of radiation is discontinuous, the energy ultimately becoming concentrated in a comparatively few discrete entities, within the cells. Only the energy liberated at these points was thought to cause any discernible effect through the relatively enormous amount of heat produced, whereas the energy absorbed elsewhere was considered to be of negligible biological significance. Since then, the point heat theory has been considerably expanded, and Crowther in 1938, on the occasion of the Twentieth Sylvanus Thompson Memorial Lecture, by correlating the newer findings, developed the so-called "target hypothesis." This theory, too, focuses attention on the discontinuous nature of roentgen-ray absorption and assumes that action takes place whenever one of the biological structures is "hit" by the radiation. But the "hit" is interpreted as the liberation of a pair of ions anywhere within the sensitive target area. Other investigators have given still different meaning to the word "hit," such as the absorption of a photon or, passage of an electron through some sensitive area.

In contradistinction to this discontinuous "point" or "hit" effect of the roentgen ray on biological objects, an action of a more generalized nature was assumed by adherents of a second theory which is most commonly known under the name of "poison theory." The general action was attributed to a photochemical effect of the radiation on the nucleus, leading to concentration of a certain poisonous material which through diffusion produces injury or death of the entire cell. Failla, in 1937, advanced the so-called "fluid flow theory," which also assumes a general effect through change in the ratio of the "radio ions" (rather than electrolytic ions) and the photochemical products on two sides of cytological membranes, thus creating a fluid flow which leads to change of cell properties.

In the following, certain experimental data will be presented which aid in throwing additional light on the mechanism of the biological activity of the roentgen rays leading us a few steps farther toward the final solution of the problem which, I am confident, one day must come. Perhaps it may not be out of place to re-emphasize here a fact known to all of us, that the human cell constitutes one of the most intricate of all biological objects. It may be best construed as a system in which hereditary elements guide various types of physicochemical activities, depending on the influence of the environment. The hereditary elements are contained in the nuclear material and, according to Henshaw, are believed to represent specific entities located in linear arrangements along the chromosomes in a manner resembling beads on a string. Each entity, or gene, may change the course of life of the cell and, if the action of the roentgen rays injures them, multipolar cell divisions may be the result, with early death in the cell progeny.

The environmental factors may be located within the cell in the cytoplasm or without in the surrounding fluid. In both instances, through a diversity of physicochemical reactions, they may incite the hereditary mechanism, setting in motion particular phases of activity in which the cellular membrane must play an important rôle. Therefore, in studying the radiation effect on the cells, it seems worth while to pay special attention to certain physicochemical reactions which may influence the equilibrium between the intra- and extracellular medium, as well as to the function of the interlying membrane. Our experiments are in connection with such phases.

In one series, solutions of proteins, similar to those which were thought to constitute the most essential elements of our cells, were subjected to roentgen irradiation and studied for a breaking up of their molecules by measuring the osmotic pressure of the solution. The pressure so obtained is actually characteristic of two things, the number of particles of the solute

in the solution, and the character of the membrane. A truly semipermeable membrane must, of course, be completely permeable to the solvent, and completely impermeable to the solute. Such a membrane is also permeable to the ions of electrolytes, and it must be expected that in the case of a protein being broken down to low molecular weight amino-acids, or of amino-groups being broken off to form ammonium salts, these ions will penetrate any membrane which will hold the protein molecules and still be permeable to electrolytes. The direct measurement of osmotic pressure to any high degree of accuracy has always been attended with so much difficulty that most investigators have preferred to calculate this value from some more reasonably simple physical measurement such as the freezing point. For our purposes, none of these indirect methods would suffice, due to the fundamental nature of protein solutions, which undergo denaturation or other serious changes rather easily with changes in physical state. Hence, a considerable amount of development work was necessary.

The final outcome was an osmometer, similar in outward form to the one developed by Frazer and Myrick, but differing in a number of important respects. This instrument, which in actual use works inside of a constant temperature apparatus, is shown both assembled and dis-assembled in Figure 1. The porous cup, which carries the membrane, is made of sillimanite and fired to the hardness of a sparkplug. On the outer surface of this cup the membrane, which may be copper ferrocyanide, viscose or other material, is deposited by the appropriate method. The body of the ap-

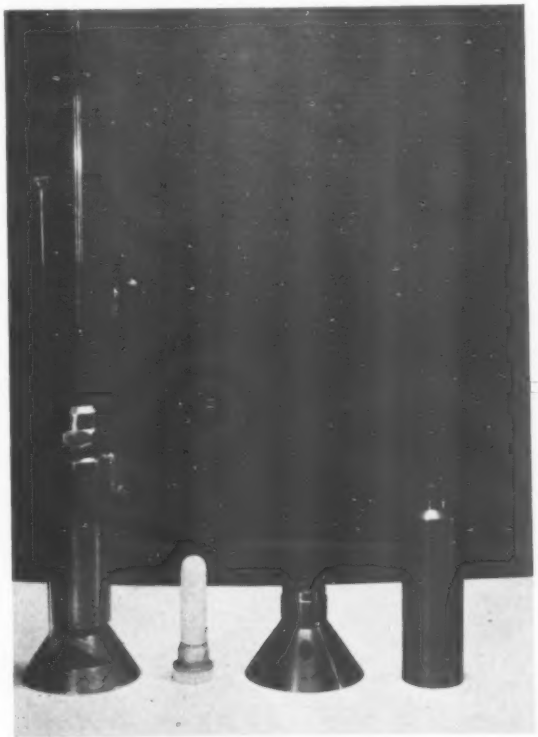


Fig. 1

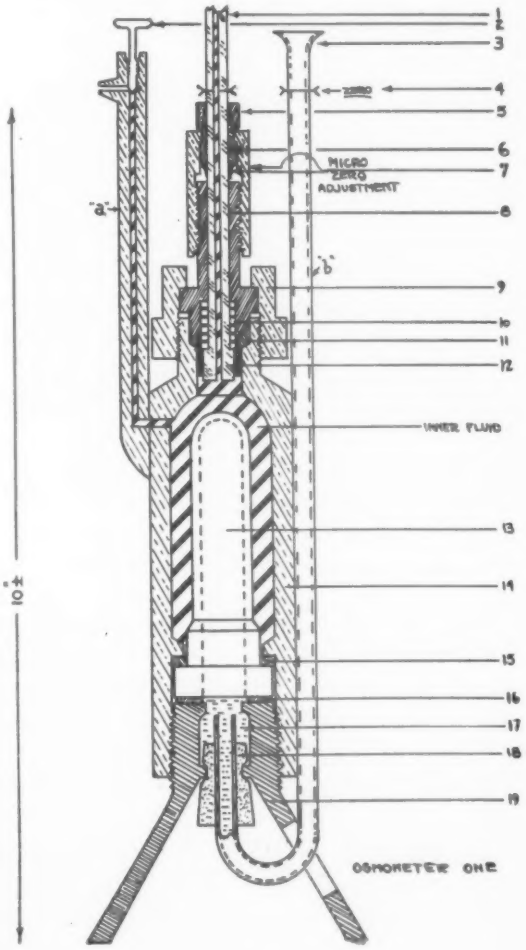


Fig. 2

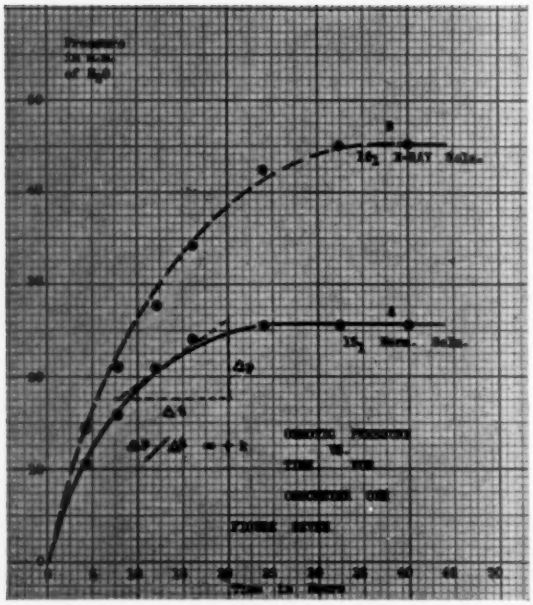


FIG. 3

paratus is a heavy brass shell, from the top of which a capillary manometer projects. The arrangement of the parts is shown in Figure 2, which is a cross sectional drawing. It can be seen that the volume of solution required is reasonably small, and particularly that the change in volume, and, therefore, the dilution error, is extremely small in proportion. A typical pair of curves for an experiment with this apparatus is shown in Figure 3. In this case, a 1 per cent solution of egg albumin in distilled water was irradiated with 12,000 roentgens at 550 kilovolts. This is, of course, a rather heavy dose of radiation but the change in osmotic pressure is 78 per cent, which is a rather startling amount. It is, however, in proportion to the dosage administered. A second osmotic pressure apparatus was used, this one built according to a design given us by Bourdillon, and using some special membrane material of a protein composition which he supplied to us. The advantage of this equipment is that it requires only a few drops of solution and works fast. It gives excellent results, and with the same membrane material will duplicate the results of the high pressure apparatus. The construction of the instrument is shown in Figures 4 and 5. This instrument was used with a different membrane, and the results shown in Figure 6 were obtained. At first glance, it might appear that some error has occurred, since the osmotic pressure of the irradiated solution is about 45 per cent lower than that of the unirradiated control. The explanation is quickly found, however, when the outer fluid is analyzed, for it contains the missing portion of the nitrogenous material. In other words, the osmotic pressure continued to rise, until the breakdown of the albumin reached a critical point. From this moment on, the membrane became permeable to the new chemical products, and the osmotic pres-

FIG. 4

sure started to decrease. A biological similarity is perhaps represented in the next two illustrations, which are stained sections from the brain of a dog. He lived for four days following the irradiation, and died in status epilepticus. The first (Fig. 7) is a specimen taken from an irradiated area in the motor cortex of this dog. The brain shows numbers of appreciably swollen cells. This intracellular edema demonstrates that the osmotic pressure within the cell has increased. The next illustration (Fig. 8) shows another section from the same dog, but at a point where the dosage was slightly larger, and here there are cells of exactly the same type and the same cortical layer, but this time, decidedly pyknotic. Originally, we thought that

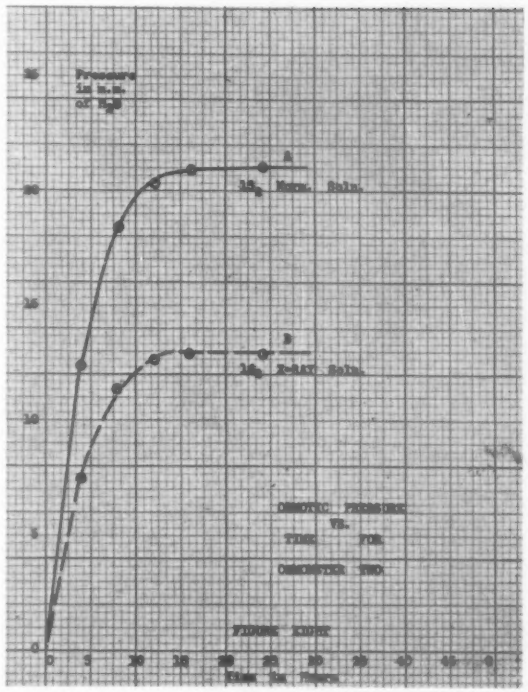


FIG. 6

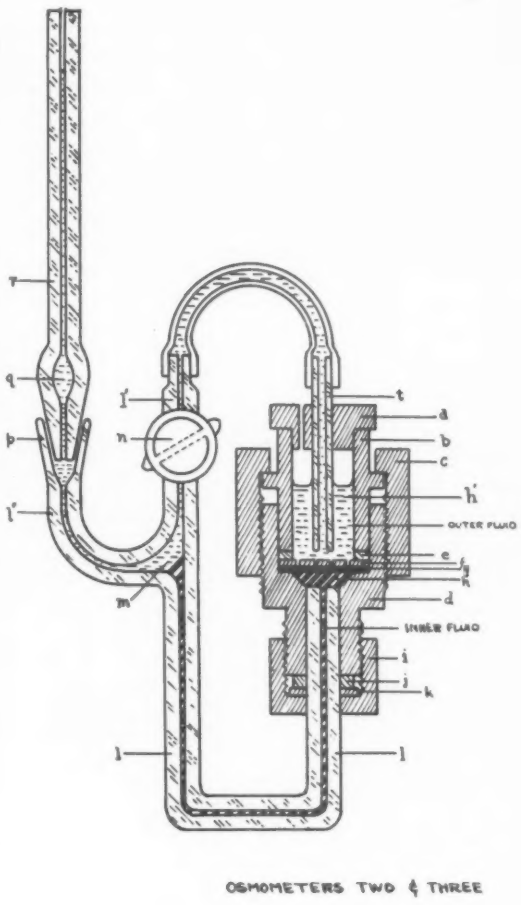


FIG. 5. Reproduced by permission from Bourdillon.[1]

these shrunken cells were the result of rupture of the cell membranes. But cells which have ruptured, probably due to excessive internal pressure, are easily found in these specimens and have quite a different appearance. The large pyknotic Betz cells shown here are not ruptured, for there is no chromatin matter outside the cell, and the walls themselves are continuous. We are led to believe, then, that a portion of the protein material within the cells was broken into such small fragments that the osmotic membrane of the cell wall could no longer hold them, as in the case of the laboratory experiment, or that the cell wall itself was affected.

Obviously, when we irradiate a biological system, we must bombard all of the parts simultaneously. Hence, the semipermeable membranes which are the cell walls are affected at the same time as the protein material which they contain. Therefore, osmotic changes may result from injury to the cell wall rather than from injury to the contents.

This leads us to the second group of experiments, which are in connection with situations similar to those observed in cell membranes. Figure 9 shows a monomolecular layer of lipoid material prepared on the surface of water and exposed to only 600 r of 550 kv. radiation. In this case, the radiation enters through the bottom of the thin aluminum pan and passes through a 2 centimeter layer of water before hitting the monolayer. In this way, the beam is brought to equilibrium with its secondary electrons. It can be seen at once that the beam, which entered through a small square portal under the pan, has imprinted itself clearly on the monolayer on top of the water.

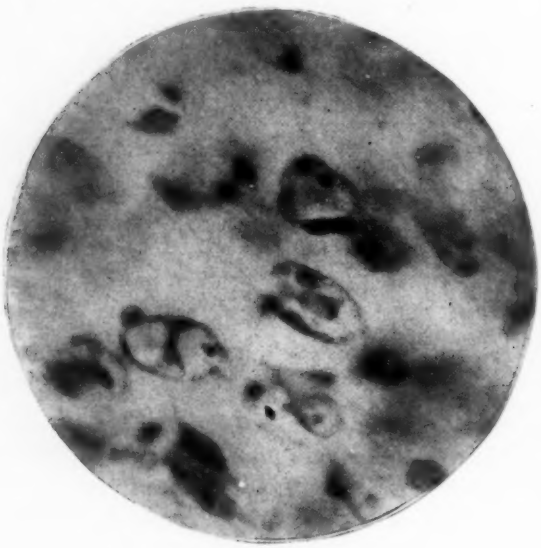


Fig. 7

Fig. 8

Monomolecular layers which are exposed to water on one side and air on the other, and then irradiated in the laboratory, show different degrees of reactivity, depending upon their own chemical nature. The layer shown, which broke up under the influence of a very small dose of radiation, was prepared from the highly unsaturated lipoid material present in lanolin. A similar monolayer prepared from a completely saturated and highly unreactive substance, such as stearic acid, requires a much greater dosage before it shows any change. It is also true that the exact physical state of the monolayer greatly affects its reaction and that, under some circumstances, reactions may be delayed so that their results appear only after the passage of time. Stenstrom and Vigness, in 1938, showed that when a drop of oil was placed on the surface of water and irradiated, it tended to spread out over the surface, and they showed further that this effect continued after irradiation was stopped, in some cases for at least twice as long as the time that the beam was on. Langmuir later showed that this was probably a direct oxidation effect. An example of such an effect is shown in Figure 10. In this case, the monolayer is like the preceding one, except that it is under somewhat greater pressure and was irradiated upon its upper surface. A dosage of 600 r of 550 kv. radiation was administered without any apparent effect. Twenty minutes later, the layer broke away, leaving an opening slightly smaller than the beam, but of precisely the same shape.

At the present time, the most important concept in quantitative biology is the idea of orientation of the protein and lipoid molecules; and this concept, for the first time, gives us a chance to understand the

biological action of radiation. Let us, therefore, consider the manner in which these molecules tend to orient themselves on a surface and form themselves together into working structures. For many years the exact spatial formulation of the smaller molecules, such as the fats and sugars, has been known. The work of Emil Fischer, and of many other organic chemists starting in the century just past, has delineated these things by a vast series of the most ingenious experiments. Only recently, how-

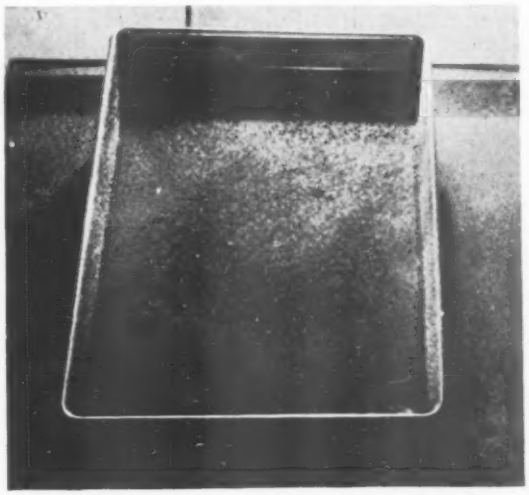


Fig. 9

ever, with the development of the precise techniques of modern physics, has it been possible to know the spatial configuration of the groups in large chemical molecules. If we take a simple aliphatic acid of a type known to be of great importance in the body, for example, stearic acid, the organic chemist can tell us that it consists of 18 carbon, 36 hydrogen and 2 oxygen atoms (Fig. 11). He can also tell us that it consists of 1 methyl group followed by 16 methylene groups connected in a long straight chain, with a carboxyl group on the end. The straight chain has all of the chemical and physical properties of a piece of paraffin, while the carboxyl group has the properties of an acid. Precise physical measurements tell us further that the chain is 38.7 Ångströms in length and 4.05 by 3.62 A.

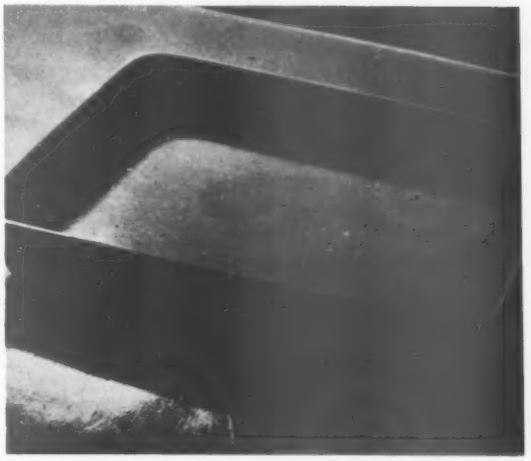


Fig. 10

in cross section. In addition, roentgen-ray diffraction measurements tell us that the distance from any one carbon atom in the chain to the next is 1.54 A., but that two succeeding spacings in the chain total 2.54 A. At first glance, this is failure of measurements to agree among themselves, but far from being a source of woe, this is precisely the type of discrepancy which delights the seeker after exact scientific truth, for it is the first clue to new knowledge. The solution of this particular problem involves physical experiments too far afield to be discussed in detail, but ends with the knowledge that the angle between single valence bonds in the carbon atom is 109° 28′. The actual appearance of Emil Fischer's straight chain then is what is seen in Figure 12.

If we take a small quantity of such a

$$C_{18}H_{36}O_2$$

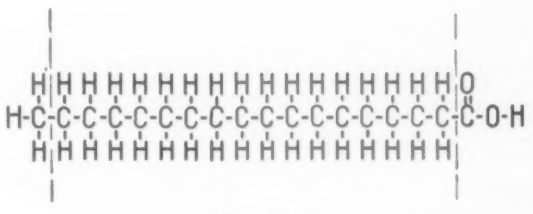


Fig. 11

substance and place it upon a perfectly clean surface of water the end, which is water-soluble, will enter into solution; we say it is "hydrophilic," but the "tail" of the molecule is definitely hydrophobic,

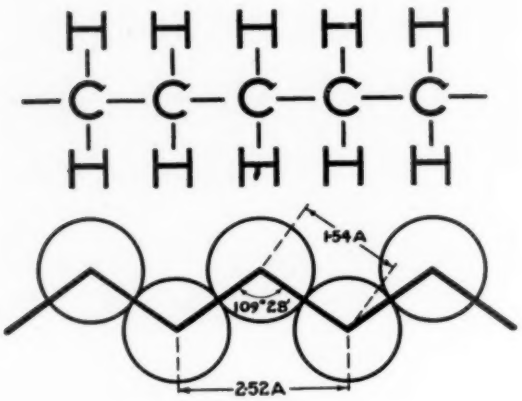


FIG. 12

and projects out from the surface. The result is a surface like the nap on velvet (Fig. 13). These molecules are called "polar molecules," due to the fact that

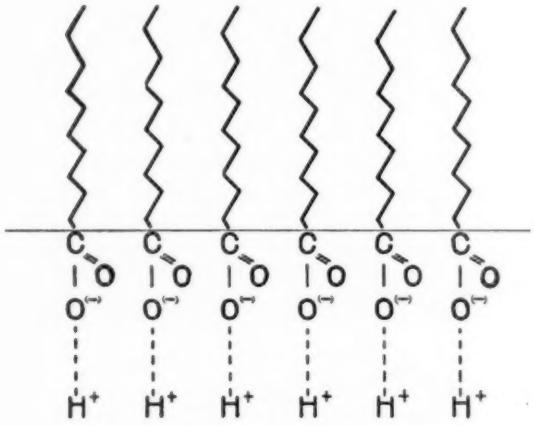


FIG. 13

they carry a group with a strong charge, electronegative in this case, on one end. They form themselves into monomolecular layers at any interface where the conditions are such that the polar end can ionize in one medium while the inert end is soluble in another; in this case, it is a water and air interface, but an interface of water and oil would serve even better.

This alignment results in what is actually a two-dimensional crystal, and if this is true, we should expect the monolayer to have a refractive index, and a mechanical strength, for the inter-molecular and inter-ionic forces in crystals are relatively great, and show themselves grossly as resistance to cleavage and compression. Such is the case with these monomolecular layers. Figure 14 shows an apparatus used by Langmuir. Weights placed on the pan, *P*, of this apparatus balance the force exerted against the monolayer at the bottom. Monolayers of different substances, of

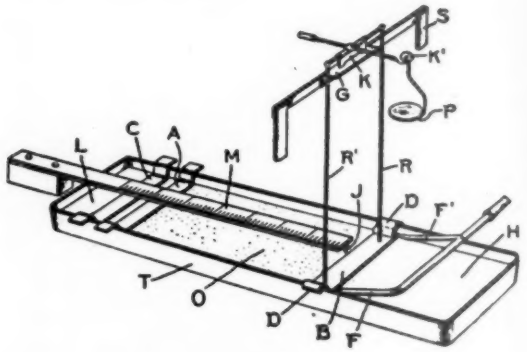


FIG. 14. Diagram of trough . . . showing surface pressure balance. Reproduced by permission from Langmuir.[8]

course, have different amounts of strength, just as one crystal may be harder to crush than another.

The facts taught us by the simple monolayer of a fatty acid help greatly when we come to consider the proteins. Here again, the chemist gave us the first basic information, but his methods could give us the precise composition of only the smaller molecular components, the amino-acid residues, which combine together to form great complex chains. These chains have molecular weights of the order of 35,000 and linkages of the greatest complexity. Chemical methods are always limited by the fact that they include hydrolysis and procedures which cause denaturization of proteins. They therefore give us the

structural building blocks without giving a picture of the building itself. Just as in the case of the simpler substances, however, roentgen-ray diffraction analysis furnishes an exact measure of the orderly spacings which occur in these molecules, and the fact that they form monolayers indicates that they consist in their natural state of molecular aggregates which can show both hydrophilic and hydrophobic groups. Figure 15 shows the form of some of the amino-acid groups of which these large protein molecules are built. The simplest one, of course, is alpha-amino-acetic acid (glycine). In the chart shown, the hydrophilic groups are to the right of the line drawn vertically through the molecular formulae. A number of very interesting things about these hydrophilic groups are immediately apparent. In the first place, every alpha-amino acid has both a negative and a positive group attached to the same carbon atom on the end of a hydrocarbon chain. Some of the more complicated ones also have either a positive or a negative one elsewhere in the chain. This gives rise to the familiar peptide linkage by means of which one of these acids can join with another. When we come to consider their solubility in water and their chemical behavior, it is obvious that they will be attracted differentially by acid or basic solutions. Figure 16 gives a diagram of the protein chain. Between the two closely spaced lines on the right side of the figure is the carbon nitrogen chain which is called the backbone of the protein molecule. From each side of this chain there are side-chains extending each way in the figure. It must be remembered that, in actual fact, this is a three-dimensional structure and not flat, as we might expect from the

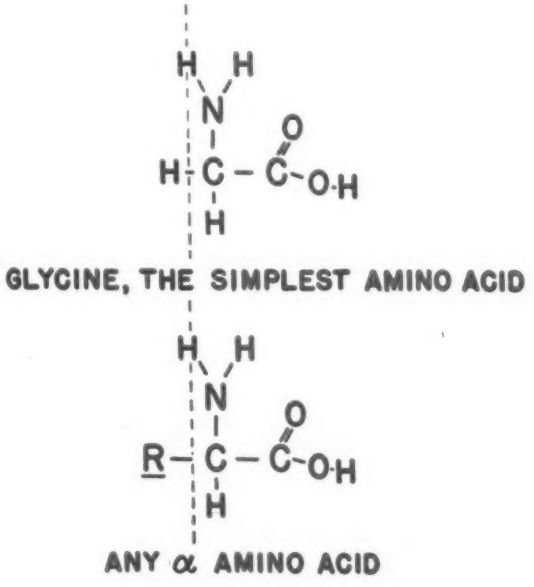


Fig. 15

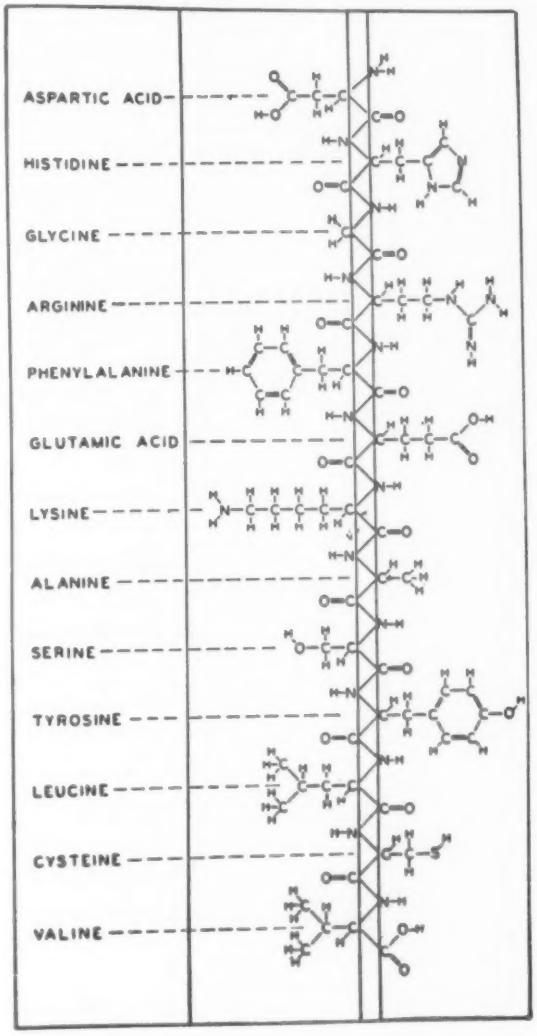


Fig. 16. Diagram of a protein chain. Reproduced by permission from Sponsler.[10]

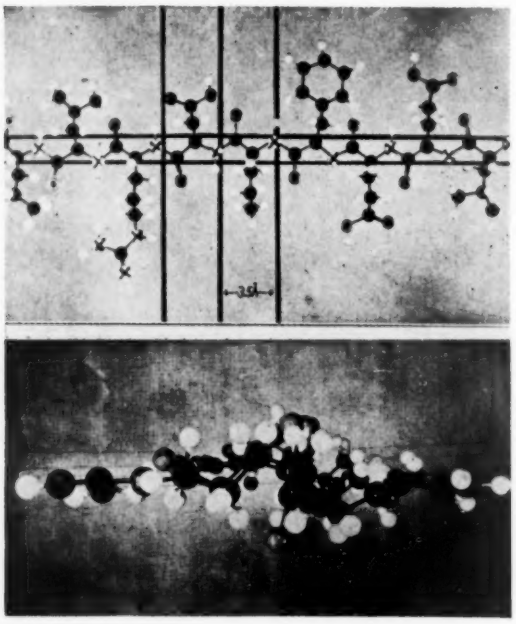


FIG. 17. (*Top*) A model of a polypeptide chain made to scale, showing eight amino acid residues. The back-bone and two residues are accentuated by the heavy lines. The black balls represent carbon atoms; those with a central dot, oxygen, and those with a central cross, nitrogen. The smaller white balls represent hydrogen atoms. (*Bottom*) An end view of a protein model. The vertical thickness in the middle is due to the back-bone and is about 4.5 Å. Reproduced by permission from Sponsler.[10]

appearance of this formula. A picture of a very accurately made scale model is shown in side view and in end view in Figure 17. When this molecule is oriented in a monolayer on the surface of water, the backbone

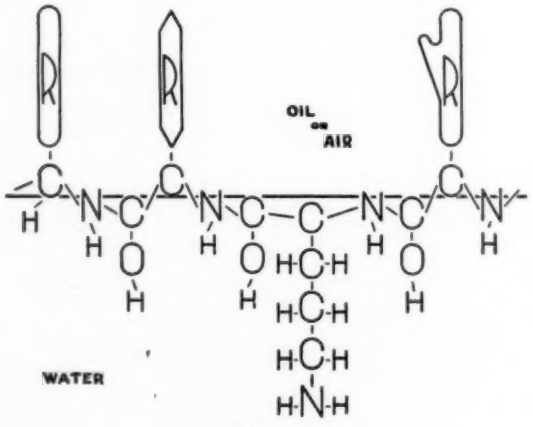


FIG. 18

lies parallel to the surface while the hydrophilic groups enter into solution, and the hydrophobic groups are repelled upward away from the surface and at angles dependent upon their valence linkage. Such an arrangement is shown in Figure 18, but now, also, there is a new situation due to the fact that there are two types of hydrophilic groups and also to the fact that, as in any straight chain compound, there can be rotation of side-chain groups around the backbone of the protein molecule. If the pH of the water is decreased

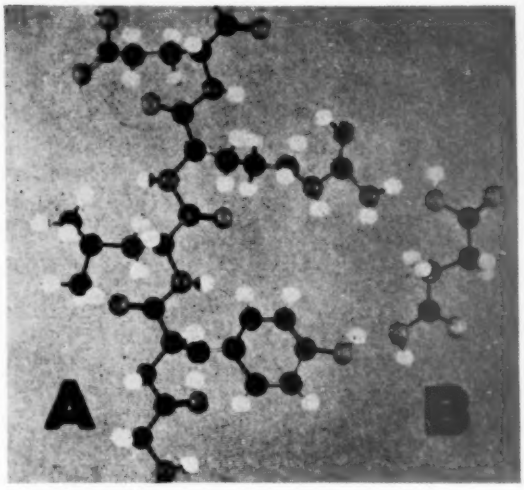


FIG. 19. Reproduction of models to show similarity of spacing, about 7 Å, which may exist between the active groups of succinic acid *B* and the terminal groups of the two residues arginine and tyrosine on the protein chain, *A*. Reproduced by permission from Sponsler.[10]

so that an excess of hydrogen ions is present, the amino groups will be strongly attracted while the carboxyl groups will be less attracted. In like manner, if we put some substance in water, which has a strong attraction for the negative groups, there will result a different spatial arrangement of the chain. This ability of the protein chain to rotate upon itself and orient possibly reacting groups together so they may combine is of the greatest importance, for in this manner not only are chemical combinations built up at the interface, but

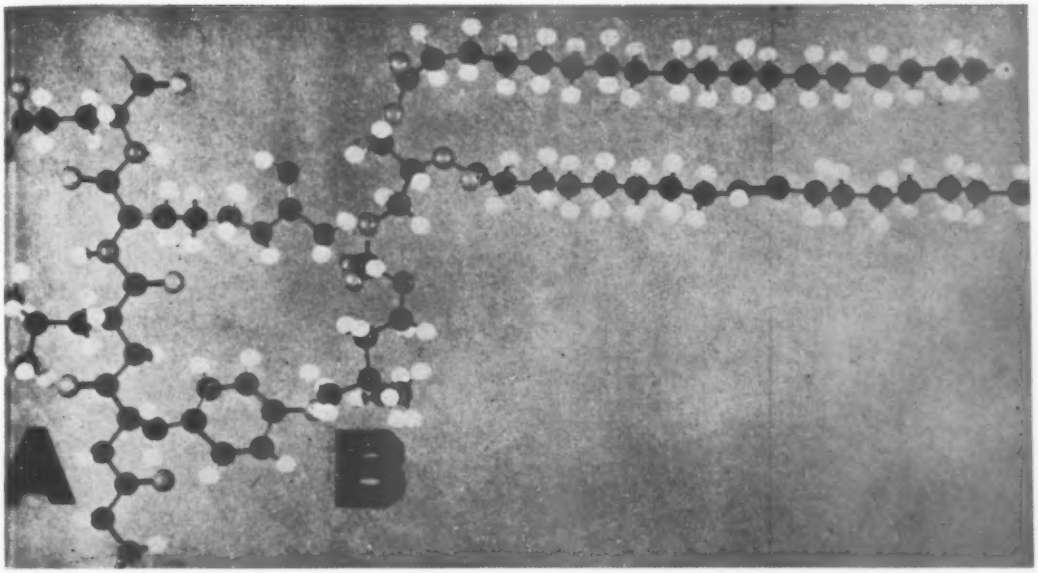


Fig. 20. Reproduction similar to that of Figure 19 except that the prosthetic group is a form of lecithin. Reproduced by permission from Sponsler.[10]

chemical combinations between molecules oriented into the same surface also occur, so that unlike the simple monomolecular layer of the aliphatic acid in which each paraffin chain projected upward like a single thread of silk in the nap of a cloth without relation to its fellows surrounding it other than to exert a repelling physical force upon them, the protein molecules combine themselves together into a continuous homogeneous sheet. The manner in which this may occur is illustrated in the following photographs of models, for which we are indebted to Professor Sponsler. Figure 19 shows at *A* a part of a protein molecule consisting of two amino-acid residues, one of arginine and one of tyrosine. Reacting groups project to the right from the backbone and at *B* a simple molecule, in this case succinic acid, joins them together. This combining group need not be anything as simple as succinic acid. It can just as well be two reacting groups on the backbone of another protein chain, having the same spacing, and arranged in the same monolayer. Or, as in Figure 20, it can be a molecule of lecithin, which is a lipoid. The fact which of all is by far the most important is that the "three musketeers" of the protein chain, the carboxyl carbon, the alpha carbon and the amino group, can shed the hydrogens of the amino and the doubly bound oxygen of the carboxyl, and thereby gain four active valence bonds. Just how this comes about is shown in Figure 21. For convenience of illustration here we have greatly reduced the scale of the larger part of the molecule and exaggerated the size of the groups of three atoms involved in the reaction. It can be seen that when two of these groups combine they form the familiar hexagonal ring, as shown in Figure 22, and this ring still has combining power remaining. In this way the whole lacy fabric, known as the "cyclol structure," is built up to the form shown in Figure 23, which is taken from the work of Wrinch. The folding of this fabric to form a three-dimensional octahedron gives the structure of the globular proteins, so beautifully shown by Wrinch (Fig. 24) (insulin).

The fact that lipoid substances will combine with protein monolayers, at last gives definite information as to the structure and the characteristics which determine

the function of the membranes of living cells. Obviously, we can form one monolayer on top of or beneath another which already exists. For example, a monolayer of aliphatic acid or lipoid may have a protein monolayer formed below it in such manner that the amino groups of the protein attach to negative groups of the lipoid, while the negative groups of the protein remain in the water. We then have an artificial cell membrane and the penetration into this membrane of either fat-soluble or water-soluble drugs and chemicals can easily be tested. To get a precise comparison between this artificial cell membrane and a natural one, we have only to find a natural cell whose membrane has the same structure, and try the same reactions on the cell. In the artificial membrane, we can determine penetration by measuring the pressure of the monolayer exerted against a barrier, such as Langmuir's balance, or by measuring the refractive index, or by applying any of the precise physical methods by which we ordinarily detect reactions between molecules or penetration of a new molecule into a structure of another molecule. The physiological comparison is made by watching the effect of the drug or chemical on an erythrocyte, a paramecium, or any cell which has a suitable membrane. Riedal has made the most careful and precise measurements of this sort, and by this means has been able to demonstrate the cell wall effects of many poisons, toxins, carcinogenic agents, and anesthetic materials. One single example of pertinent chemical knowledge which can be drawn from this type of investigation is perhaps not out of order. There is a well known correlation between fat solubility and anesthetic properties of certain chemical agents. Studies have also been made on arterial and venous oxygenation of the cerebral circulation of patients under the influence of these anesthetics, and it is known that the consumption of oxygen decreases far in excess of what is to be expected simply on the basis of the brain and body being at rest. If now we take a double lipoid protein monolayer and treat it with this same anesthetic agent—in this case, cyclopropane—we find that the oxygen transmission of the interface is vastly reduced. In similar manner, various anesthetic agents have been studied, both on artificial monolayers and on individual

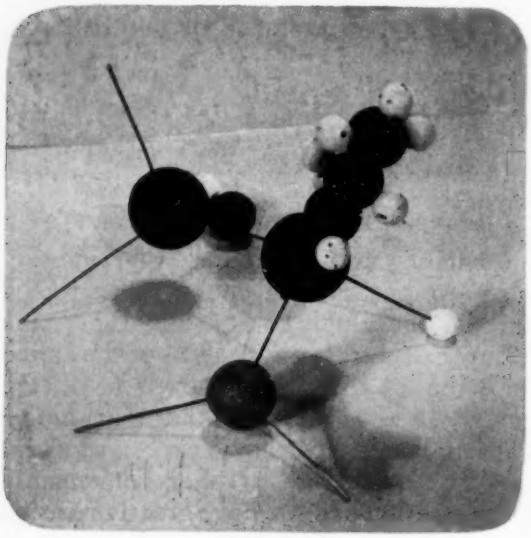


FIG. 21

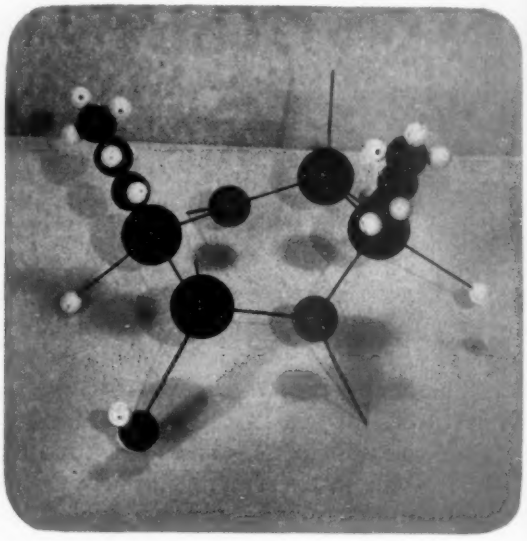


FIG. 22

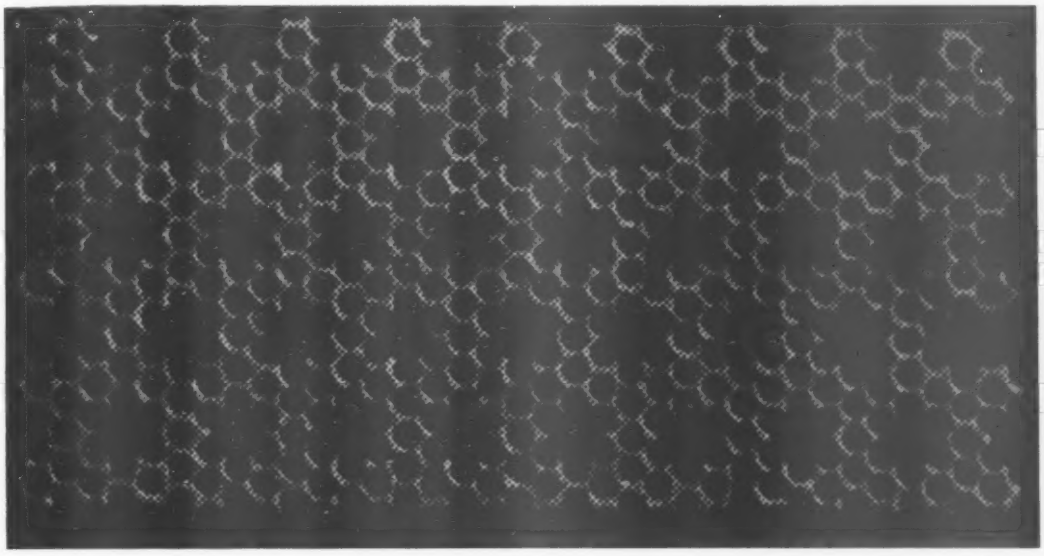


Fig. 23. The fragmentation of the cyclol fabric into oriented polypeptide chains. Reproduced by permission from Wrinch.[12]

cells. From the purely physical point of view, probably a more interesting fact is that in the monolayer there is an array of positive and negative molecular poles precisely lined up and oriented against each other. Obviously, an electrical potential must exist across the interface, and in the normal resting state this potential will be equalized by an arrangement of the free molecules on each side of the interface, so that this potential is brought to zero. This, however, is not a state of chemical neutralization but a dynamic state analogous to a battery without connections or a charged condenser. Through these studies, for the first time, it has become clear how the electrical potentials which seem to be the vital driving force, not only of the brain and nerve, but of all physiologically reactable components of the body structure, have their origin.

This brief outline of a few of the salient features of modern physical research on cell structure gives a general picture of the nature of cell membranes (and, as we shall show below, of a few intracellular structures). We see that they are not inert shells like the chitinous covering of the body of an insect, but are dynamic, living entities having a complex structure both chemically and electrically. This structure is maintained in a somewhat precarious state of balance and can change in response to small physical and chemical changes of the environment. The disruption in this state of dynamic balance, which can be caused by ionization due to an energetic secondary electron plunging through these structures, may well be imagined.

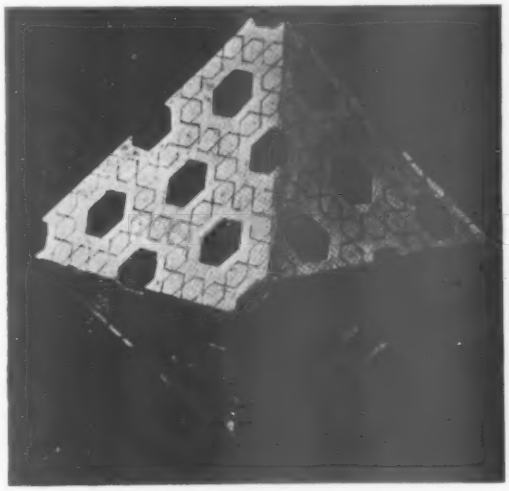


Fig. 24. The cyclol cage molecule, C_2, comprising 288 residues in its skeleton. Reproduced by permission from Wrinch.[12]

A good experimental example in this respect is the lipoid, lecithin, one of the most important constituents of brain and nerve tissue. It is a highly polar molecule, which lends itself readily to the formation of monolayers or to the formation of highly oriented multilayers on glass. A layer of this substance built up in this way has very strong optical properties and its interference with a beam of polarized light is very clear and strong. If we build such a multilayer and expose it to radiation, we should expect any disruption in the molecular or intermolecular structure to show itself by disruption of the optical properties. The effect of roentgen irradiation on such an artificial multilayer is shown in Figure 25. Here, there is a layer of lecithin about 0.05 mm. thick which was exposed to a beam of radiation, 0.5 mm. in diameter, at just one point on its surface. The two upper fields in the figure show the same point in its normal state and oriented at two opposite critical angles to the plane of polarization of the light. The third field below is a photomicrograph of the point of irradiation, and it can be seen that at the exact point where the beam struck, the molecular arrangement of the multilayer is completely destroyed. Surrounding this point, a new orientation has sprung up. A similarity may be observed in the protein material of the nerve cell or the neurone axis cylinder, but even more strongly optically active in the living nerve cell is the myelin sheath which surrounds the neurone. The myelin substance is strongly birefringent, and is known to consist of lipoid molecules with their molecular axes oriented at 90° to the long axis of the neurone. At the junction of the axis cylinder and the myelin, there is one lipoid protein interface, and on the outside of the nerve sheath, there is another. This structure is quite susceptible to injury from radiation. Figure 26 shows myelinated tracts in the brain of an experimental animal exposed to 1,200 r of 550 kv. radiation. In this figure, on the right is seen a field from normal, unirradiated hemisphere showing several myelinated fibers, and on the left a similar field, taken from an identical spot in the opposite hemisphere, which was exposed to radiation. It can be seen that, although the cytoarchitectural structure remains intact, the myelin sheath has lost a great deal of its optical activity.

During the past several years we have been investigating the effects of roentgen radiation on normal brain tissue, using dogs for experimental animals. Very briefly we may review this work by saying that it was shown that the myelin was rather sensitive to the radiation. The cells of the brain, being a non-proliferating type of cell, were expected to be radioresistant, and this proved to be the case, to about the degree expected. The ease with which we obtained myelin damage, however, gave the brain as a whole considerably more radiosensitivity than was to be predicted on the basis of the old belief that the brain is highly resistant to irradiation.

The myelin of the brain we now know to be made up of multilayers of protein and lipoid molecules arranged in a very precisely oriented structure. As is to be expected, this structure has strong optical activity, and may easily be studied in polarized light. We found that there were a number of advantages in the use of polarized light, either as an adjunct to the regular staining methods, or sometimes in preference to them. Staining methods require the complete dehydration and defatting of the specimen and in this series of radical chemical operations some of the brain structures are quite completely changed. In the polarized light method of observation, the specimen is not treated with any chemicals. In addition, we found that brain damage began when the myelinated nerves lost their optical activity, even though they retained their outward physical form. This phenomenon is illustrated in Figure 27, which shows, on the right a field in the irradiated area of a dog's brain and, on the left, a field from an identical area in the opposite hemisphere

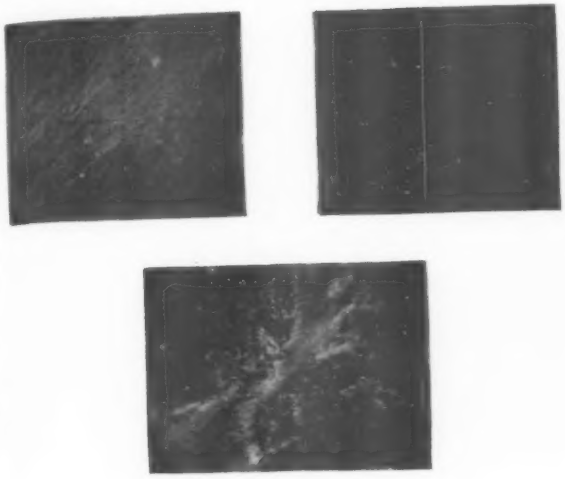


Fig. 25

Fig. 28

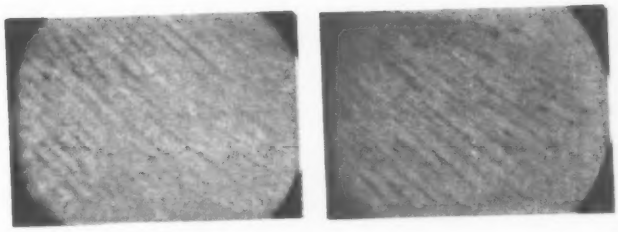


Fig. 26

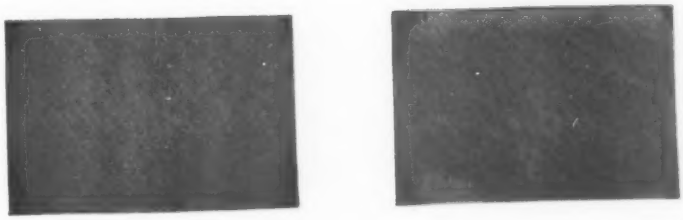


Fig. 27

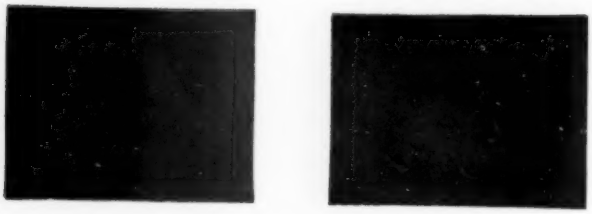
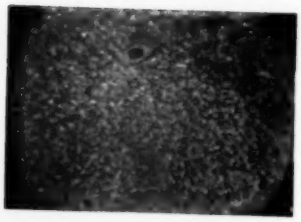


FIG. 29

FIG. 30



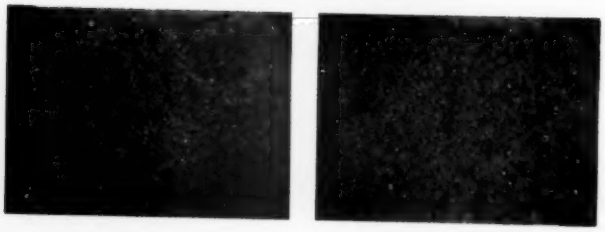


FIG. 31

of the brain of the same dog. The myelin is "stained" with the bright blue-green light of its own interference color in the polarized field of the petrographic microscope. In the irradiated area, the ability of the myelin to influence the polarized light is greatly reduced.

When we apply this method to the study of the human brain, we face certain complicating factors, due to the fact that we are dealing with a diseased brain. Some of the features observed in radiation damage are also seen in damage caused by pressure and diminished blood supply in a brain invaded by a malignant tumor; for example, in either case we find the disruption of the gross structure due to edema, and peeling of the myelin with formation of myelin ovoids. The following case, however, demonstrates that their radiation effect on the myelin can be distinguished even in the presence of complicating factors.

The patient had a deep-seated tumor (glioma) in the left temporal region which Dr. Schrieber, the neurological surgeon, considered inoperable. Two courses of high voltage radiation therapy were administered. Following the first series, the patient made a marked temporary improvement and returned to work. Four months later, he suffered a return of symptoms and was again given radiation therapy. There was no response to this treatment, and at autopsy an extensive infiltrating glioma was found. Figure 28 shows the histopathological appearance of the tumor at this time. Figure 29 shows the appearance of the myelinated tracts in the uninvaded hemisphere, in polarized lights. It can be seen at once that the myelin has assumed what we call, for lack of a better term, a "moth-eaten" appearance. It has lost optical activity in spots along the length of the fibers.

The second case is also an example of myelin degeneration. At operation, this patient had a large vascular glioma in the left temporal region. It was impossible to completely enucleate the tumor, and the patient was referred for radiation therapy. Three series of radiation treatments were given. Following the first course, the patient showed marked improvement and returned to work. Four years later, he had a marked return of symptoms, and the tumor at this time was not responsive to treatment. The patient came to autopsy, and sections were taken both from the tumor and from the brain tissue of the opposite hemisphere. The histopathological appearance of the tumor at this time was the same as that shown in the preceding case.

Myelin damage of the type demonstrated in our experimental animals is shown to be present in the remaining normal brain tissue, which is shown in Figure 30. This is the outstanding example of this type of myelin degeneration that we have been able to obtain in human material up to this time. The myelin degeneration which follows radiation injury may take as much as a year to develop in an experimental animal. For purposes of rough comparison, we say that a dog lives six to seven times as fast as a man. It is interesting to consider in this connection that after four years the white matter tracts in the cerebral hemisphere opposite to the tumor had changed in this patient to a state in which, although their outward appearance was little changed, their optical activity had completely disappeared. This is shown in the upper two frames of Figure 30. These two fields may be compared to the lower frame, which is taken from normal brain tissue.

Figure 31 is an irradiated case which was a recurrent meningioma, rather than a glioma. The upper field shows the brain at a junction between white and gray matter, with the entire area infiltrated with compound granular fat cells. The two lower frames are of one field in the white matter. The specimen was rotated 90° on the stage of the microscope to show both of its interference colors in the beam of polarized light. The optical activity of the myelin is greatly reduced.

The important point in all of these cases

is the fact that the structures which depend for their functional properties on a highly organized system of polar molecules, the oriented lipoprotein layers of the myelin or the monolayers of the cell membranes, lose their organized structure and their optical activity when they are bombarded with high energy radiation. From animal experiments, we know that when the structural organization is gone, function is gone with it, and forever.

In the course of these considerations, I have tried to show one of the directions along which modern research is leading us. What we know as modern clinical medicine today could not come into existence until the cellular structure of the body and of invading organisms was thoroughly understood. In the application of chemical drugs we use compounds which affect the cells. It is only within the last few years that anyone has been particularly interested in the precise manner in which the cells are affected, but today we consider it of the greatest importance to know whether a drug acts by chemically tying up some part of the cell structure, by interfering with the oxygen metabolism of the cell, or by some other and more devious means, In applying roentgen radiation as a therapeutic agent, we are making use of a powerful medium which can only exert its force on the cell structure of the body by taking disruptive and destructive action against the submicroscopic structures of which those cells are composed. By the study of this agent and its action, coupled with the appropriate physical and chemical studies from which it cannot logically be separated, we may come to know these submicroscopic structures as well as today we know the cells. We cannot predict presisely to what point these researches will lead us in practical clinical medicine any more than the early workers in histology could predict the clinical medicine and radiology of today, but just as the elucidation of cell structure was the great foundation of the past, so in all probability is the study of submicroscopic structure the great research of today.

The radiologist may not make any contributions to these fundamental observations, but his practical mind leads him to experiment with and use them, and out of such use may come results which will be beneficial.

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SKELETAL AND PULMONARY METASTASES FROM CANCER OF THE KIDNEY, PROSTATE AND BLADDER

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NEW YORK, NEW YORK

THE literature contains few references to the subject of pulmonary metastases from cancer of the kidney, prostate and bladder, but it is abundant on skeletal metastases from these malignancies. The earliest reports, although they established the existence of these metastases, are not correct as to their incidence. This is understandable since the findings were based on postmortem material and many sites of spread of the primary tumor must have been overlooked. Later reports depended on roentgen findings, before the roentgen ray had reached its present technical excellence, and are probably inaccurate. Communications in the more recent literature are not subject to the above criticisms, but the total of cases reported are too few for exact figures as to the incidence of these metastases.

This paper has been written in the hope that the addition of our material may help clarify questions that still exist as to the frequency of these involvements. The patients at the Montefiore Hospital for Chronic Diseases were especially suitable for this investigation. The majority reached the hospital in the late stages of the disease and, in almost all instances, careful workup was possible before death. In addition, a large percentage also had postmortem examination. In order to obtain the most accurate picture possible of these extensions, only patients who died were included in this study. In this way we were able to visualize all phases of metastatic growth.

SKELETAL METASTASES

Kidney. Eighty-seven cases of carcinoma of the kidney were studied. Since the differentiation of hypernephroma from vascular carcinoma with clear cells is frequently difficult, no attempt was made to separate them and they were grouped together. With few exceptions, however, the neoplasms were hypernephromas. In 39 instances (45 per cent) roentgen or postmortem examination revealed skeletal metastases (Fig. 1).

Albrecht,[1] in 1905, and Gottesman and co-authors,[20*] in 1932, reported skeletal metastases in nearly half of their cases.

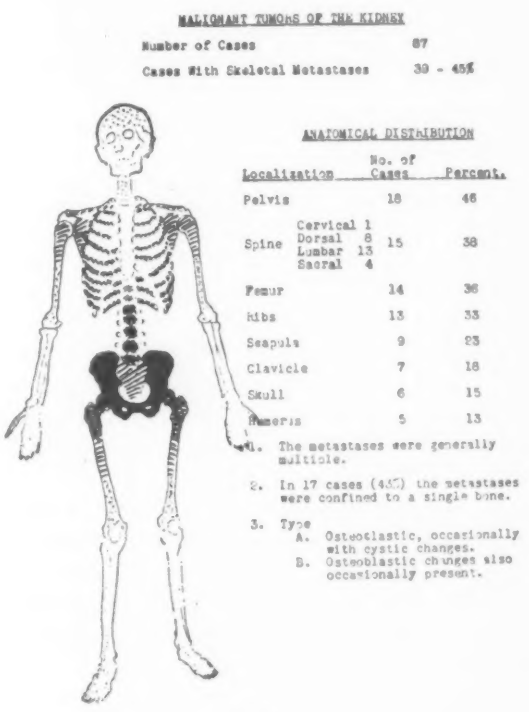

MALIGNANT TUMORS OF THE KIDNEY
Number of Cases 87
Cases With Skeletal Metastases 39 - 45%
ANATOMICAL DISTRIBUTION
Localization
No. of Cases
Percent.
Pelvis 18 46
Spine Cervical 1 Dorsal 8 Lumbar 13 Sacral 4 15 38
Femur 14 36
Ribs 13 33
Scapula 9 23
Clavicle 7 18
Skull 6 15
Humerus 5 13
1. The metastases were generally multiple.
2. In 17 cases (44%) the metastases were confined to a single bone.
3. Type
A. Osteoclastic, occasionally with cystic changes.
B. Osteoblastic changes also occasionally present.

FIG. 1.

Copeland,[12] however, found the incidence to be 34.9 per cent, and Turner and Jaffe[39] reported only 20 per cent. Other authors

* Dr. Gottesman analyzed much of the material at the Montefiore Hospital up to 1932, and some of his cases have been included in the present report.

FIG. 2. Case 1. Metastases to the right humerus from hypernephroma. Soft tissue swelling, extensive bone destruction and pathological fracture of the proximal portion of the right humerus.

have described bone involvement from kidney tumors but do not give percentages. These figures would certainly indicate a marked predilection for bone metastases from hypernephroma.

The anatomical distribution of the metastases is given in Figure 1. This shows the axial and trunk bones to be more frequently involved than are the bones of the limbs. With some exceptions, this corresponds rather closely to the findings of Copeland,[12] Sutherland and co-authors,[37] and Schinz and Uehlinger.[33] Pathological fractures are not infrequent and were observed in 7 instances, 5 in the femur and 2 in the humerus. Whereas skeletal metastases from tumors which have a predilection for bone are often multiple, this is not always the case with hypernephroma. In 17 instances, 43 per cent of the group, the lesions were confined to a single bone and to a single area in that bone. Schinz and Uehlinger[33] reported single metastases in 6 out of 20.

Frequently the kidney tumor is silent, and metastasis to bone is the first indication of the presence of a malignant growth. In some of these patients the roentgen appearance simulates a primary bone tumor. Attention was first focussed on such cases by Albrecht[1] in 1905. Scudder,[34] in 1906, Halstead,[24] in 1907, Gibson and Bloodgood[18] and Joll,[26] in 1923, Gottesman and co-authors,[20] in 1932, and others have stressed this feature. Two illustrative reports follow:

CASE 1 (Hospital No. 28453). M.P., female, aged sixty-nine, had severe pain in the right arm, of six months' duration. She was treated for neuritis by several physicians before a diagnosis of a bone growth was finally made and she was referred to Montefiore Hospital. On admission, she presented a tender fusiform swelling of the upper third of the right humerus. Roentgen examination of this area showed soft tissue swelling, extensive bone destruction, and a pathological fracture of the upper third of the right humerus (Fig. 2). Except for a slight secondary anemia, a l laboratory examinations, including the Bence-Jones test, were negative. High voltage roentgen therapy to the involved area was followed by disappearance of the soft tissue swelling and marked relief of pain. A few months later, metastases appeared in the pelvis, upper right femur, lungs and pleura. The postmortem examination revealed a small,

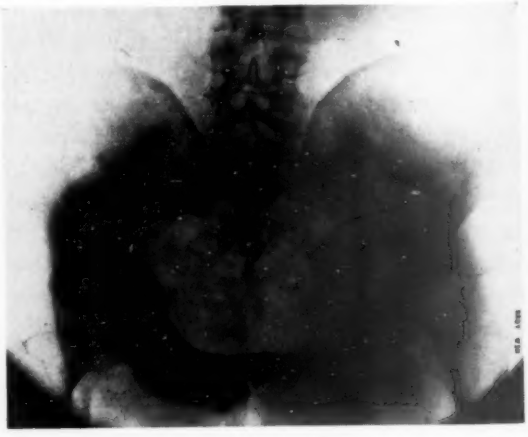


FIG. 3. Case 11. Metastases to the pelvis and right femur from hypernephroma. There is extensive bone destruction of the right ilium, ischium, pubis and head of the right femur. The lesion has some resemblance to a multilocular cyst.

silent hypernephroma in the left kidney with metastases to the lungs, pleura, pericardium and suprarenal glands.

CASE II (Hospital No. 15824). C.F., male, aged seventy-one, sought treatment for pain localized to the right groin and buttock. He was first told he had rheumatism. Later, roentgenograms were taken and the diagnosis changed to Paget's disease. Pain persisted, and the right upper thigh became swollen and a large, deep, fixed mass could be palpated in the right lower quadrant. He was re-examined; a diagnosis was made of giant cell tumor of the pelvis and he was referred to Montefiore Hospital for radiotherapy. Roentgenograms now revealed, in addition to Paget's disease of the pelvic bones, marked destruction of the right ilium and sacrum (Fig. 3). The extensiveness and osteolytic character of the lesion, and the fact that no other bones were involved, caused us to make a tenative diagnosis of metastatic hypernephroma. A kidney tumor, however, could not be demonstrated. He was given intensive radiotherapy with partial relief of pain. Fifteen months later, biopsy at another institution, was positive for hypernephroma.

Roentgen Characteristics. The lesions may be multiple or single. They are always destructive in character and rarely produce new bone. The earliest sign is an area of rarefaction in the medullary portion of the bone. As the growth progresses, the cortex may expand. At times, the external appearance is that of a simple cyst produced by the metastasis breaking through the cortex of the bone, with the formation of local cystic growths, occasionally pulsatile (Fig. 4). The metastases have a predilection for the upper ends of the long bones, the regions of the nutrient vessels. It is noteworthy that when the pelvis is involved, the upper third of the femora frequently has lesions. Geschickter and Copeland[17] have noted, and it is also our impression, that the small silent hypernephromas give rise to more extensive bone involvement than the larger kidney growths. However, we believe this to be due to the fact that the small silent lesions are not as fulminating as the larger growths and therefore the survival period is greater in the former group.

FIG. 4. Atypical metastasis to the skull from hypernephroma. The metastasis has broken through the internal and external plates of the frontal and parietal bones to produce a swelling which on palpation felt like a cyst. Vertical new bone formation extends into the mass.

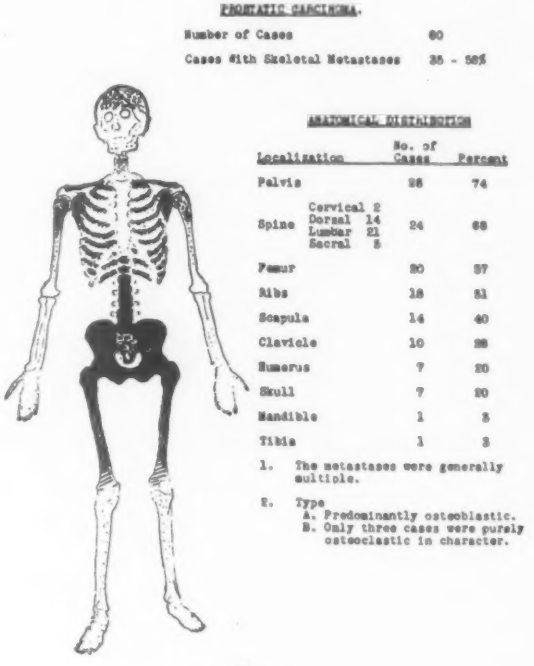


FIG. 5.

Prostate. The first recorded case of skeletal metastases from carcinoma of the prostate was by Thompson,[38] in 1854. However, very little was known of these

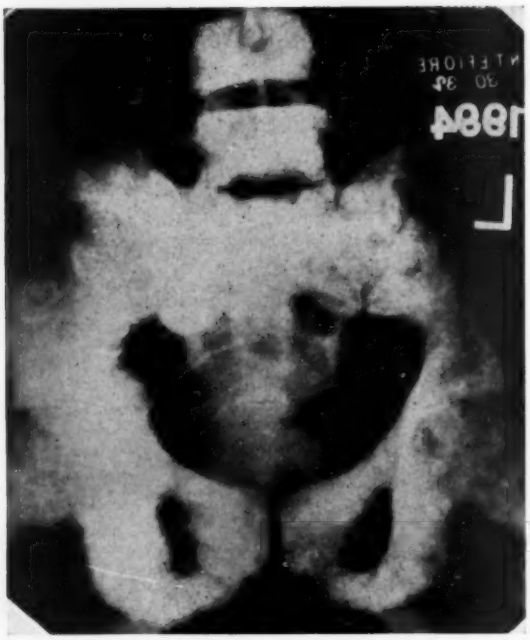


Fig. 6. Osteoplastic metastases from carcinoma of the prostate. Extensive laying down of new bone in the lumbar spine, pelvis and femora.

metastases until von Recklinghausen,[32] in 1891, published the first complete work on this subject. More recently, the contributions in this field have been frequent and of great interest.

We investigated 60 patients with carcinoma of the prostate and in 35 (58 per cent) there were found skeletal metastases

Fig. 7. Metastases from carcinoma of the prostate. In contrast to Figure 6, the metastases appear as small islands of dense bone. Superficially there is some resemblance to osteopoikilosis.

(Fig. 5). Bumpus,[7] in 1921, reported skeletal involvement in 41 patients (30 per cent) out of 135 with roentgen examination. Copeland,[12] in 1931, studied 1,040 cases. Only 50 per cent of these had roentgen studies and of this number, 25 per cent were positive. Sutherland,[37] in 1932, found the bones positive in 296 (28.6 per cent) of the patients examined. Our figures are identical with those of Turner and Jaffe,[39] who reported involvement in 57.8 per

Fig. 8. Osteoclastic metastasis from carcinoma of the prostate. Areas of bone destruction with no evidence of new bone formation are present in both femora and both ilia.

cent of 95 autopsies. Among the highest figures are those of Kaufmann,[27] who reports a small group of 24, in 16 (67 per cent) of whom there were skeletal metastases. We found the pelvis, spine, femur, ribs, scapula, clavicles, humerus and skull, in the order named, the bones most frequently involved.

As with kidney tumors, the lesions in the bones may be the first indication of a malignant growth.

Roentgen Characteristics. The metastases are essentially osteoplastic in character, but small areas of bone destruction are also generally present (Fig. 6). Rarely, the metastases present themselves as small areas of dense bone, of varying size, scattered throughout the marrow spaces (Fig. 7). In only 3 instances were purely osteoclastic changes observed (Fig. 8).

The osteoplastic nature of these metastases has been the subject of study by a number of authors. Recklinghausen[32] has described the histopathological process as a carcinomatous osteitis. The tumor cells lodge in the capillaries and venules, cause stasis and hemorrhage, which is then followed by reactive growth of osteoid and, finally, osseous tissue. Goetsch[19] and Axhausen[2] believe that some unknown chemical irritant emanating from the tumor cells acts on the old bone and stimulates proliferation. Others state that the invasive powers of the metastatic tumor are so moderate that proliferation of bone keeps up with destruction by the tumor. The recent work in the field of serum phosphatase gives new weight to the latter theory. Gutman, Sproul and Gutman[23] have shown strikingly increased phosphatase activity of bone at the site of osteoplastic skeletal metastases in a patient with carcinoma of the prostate gland. This observation is in accord with the view, derived from pathological studies, that the mechanism of bone formation in metastatic osteoplastic neoplasms is fundamentally the same as that of normal bone formation.

Bladder. The literature on the subject of skeletal metastases from carcinoma of the bladder is both vague and limited. The earliest reports consisted of isolated cases (Clutton,[11] Wells,[40] Pic *et al.*,[31] Christensen,[10] Livingston[30]). In 1922, Kretschmer[29] reported 3 cases, Sutherland *et al.*,[37] in 1932, 9 cases, Graves and Militzer,[21] in 1934, 5 cases, Greenfield,[22] in 1941, 3 cases, and Herger and Sauer,[25] in 1942, 4 cases. The Carcinoma Registry of the American Urological Association[8] published 902 epithelial tumors of the bladder. Metastases were found in 72, or 8 per cent. Of the latter number, the bones were involved in 34. If we consider the original group of 902, the skeleton was positive in 3 per cent of the cases. The bones most frequently involved were the lumbar spine, pelvis and femora, in the order stated.

Spooner,[36] on the other hand, in 1934, in a review of the material from the Mayo Clinic from 1914 to 1931, inclusive, found invasion of the bone, except by direct extension, to be an uncommon feature. This is also true of the material from the Johns Hopkins Hospital reported by Copeland[12] in 1931, and of the material from the Montefiore Hospital. In our group, bone involvement was present in 6 cases but in only 1 instance were true metastases observed (Fig. 9). In the other cases, the pelvis was invaded by direct extension from the primary tumor.

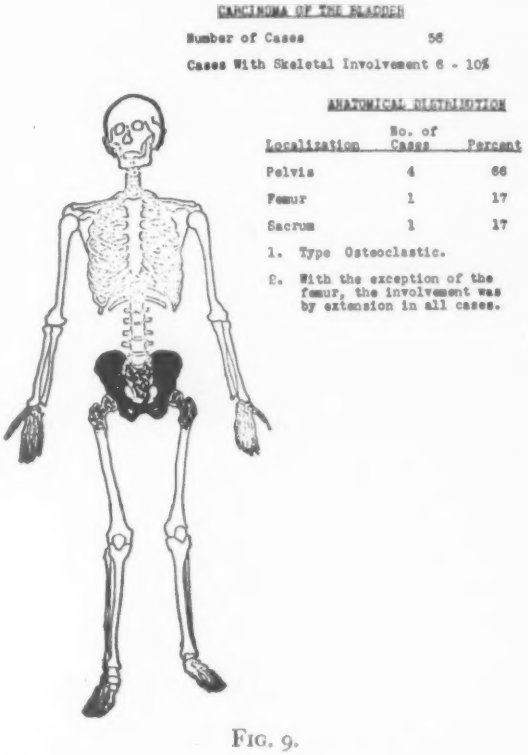

CARCINOMA OF THE BLADDER
Number of Cases 56
Cases With Skeletal Involvement 6 - 10%
ANATOMICAL DISTRIBUTION
Localization | No. of Cases | Percent
Pelvis | 4 | 66
Femur | 1 | 17
Sacrum | 1 | 17
1. Type Osteoclastic.
2. With the exception of the femur, the involvement was by extension in all cases.

FIG. 9.

From what has been written on this subject, one can therefore conclude that skeletal metastases from carcinoma of the bladder, while infrequent, do occur. In the cases cited from the literature, the involvement was practically always osteoclastic.

Therapy. Our experience with skeletal metastases from carcinoma of the bladder is so limited that this discussion will be confined to the radiotherapy of bony

extensions from carcinoma of the prostate and kidney. To properly plan treatment, it is necessary to consider both the extent of the lesions and the stage of the disease. If the metastases are widespread, the treatment is limited to the sites causing symptoms, or to areas where fracture of the bone is impending. Where visceral metastases are also present, this palliation is the entire therapeutic aim. On the other hand, if the metastases are few in number, as in hypernephroma, intensive treatment is advisable to achieve more lasting control of clinical symptoms.

Contrary to our experience in treating skeletal metastases from cancer of the breast, little if any healing of bone follows the irradiation of these lesions. The improvement that takes place is almost entirely relief of pain. In prostatic cases, the osteoplastic appearance of the bone is generally not altered; if destruction is present, some new bone may be laid down. In patients with hypernephroma, if the metastases respond to treatment, the area of destruction shows little change, otherwise it may increase in size.

Whereas in breast metastases, symptomatic relief and healing of bone can often be accomplished by moderate dosage, this is rarely so with kidney and prostate cases. These patients usually require intensive treatment with high voltage, with total dosages of 2,000 to 3,000 r per field over one or more fields, to control pain.

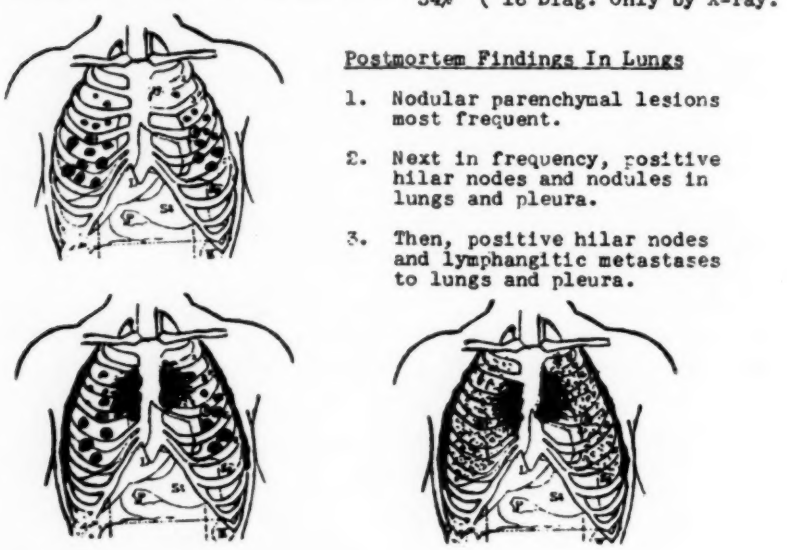

MALIGNANT TUMORS OF THE KIDNEY
Pulmonary And Pleural Metastases.
Total Number Of Cases 87
Total Number Of Postmortems 59
Total Number Of Pul. or Pl. Met. 47 - 54% (31 Verified at P.M. (16 Diag. Only by X-ray.
Postmortem Findings In Lungs
1. Nodular parenchymal lesions most frequent.
2. Next in frequency, positive hilar nodes and nodules in lungs and pleura.
3. Then, positive hilar nodes and lymphangitic metastases to lungs and pleura.

FIG. 10.

PULMONARY METASTASES

In contradistinction to the voluminous literature on the frequency and character of skeletal metastases from cancer of the genitourinary tract, little mention is made of the pulmonary spread from these tumors. The incidence of pulmonary involvement in our group, and comparison

with some of the reports in the literature, should therefore be of interest to roentgenologists and urologists.

Kidney. Albrecht[1] found the lungs involved in all his advanced cases of renal cancer. Willis[41] states that it occurs in 75 per cent of kidney neoplasms. Albarron,[14] however, reporting on 249 cases, discovered pulmonary metastases in only 75, or 30 per cent. Recently Turner and Jaffe[39] reported pulmonary metastases in 40 per cent of 25 autopsies.

We investigated 87 cases and found

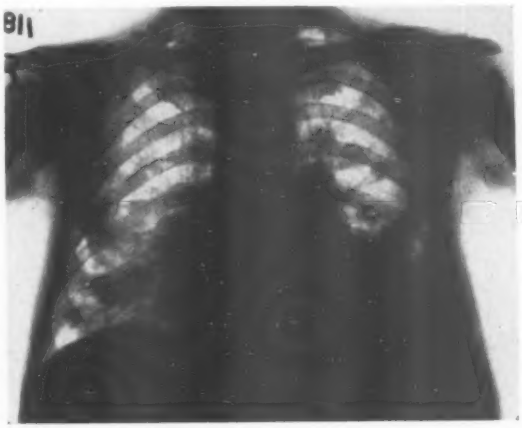


FIG. 11. Parenchymal and pleural metastases from carcinoma of the kidney. Large nodular metastases are scattered throughout both lungs, most numerous at the bases. A small effusion is present on the left side.

pulmonary or pleural metastases present in 47, or 54 per cent (Fig. 10).

For purposes of classification, the lesions have been divided into those of the parenchyma, pleura, and mediastinal or hilar lymph nodes. The parenchymal lesions were by far the most frequent. They usually consisted of fairly large, sharply outlined nodules, most numerous in the lower two-thirds of the lungs (Fig. 11). Widespread miliary lesions were also seen (Fig. 12), and occasionally enlarged mediastinal and hilar nodes were observed (Fig. 13). In some instances, the tumor broke through the gland capsules and infiltrated the lung, giving a roentgen ap-

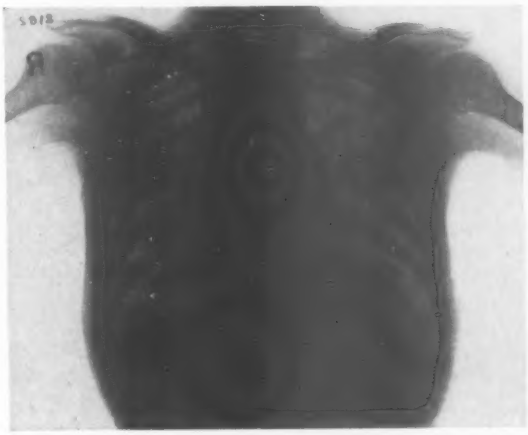


FIG. 12. Widespread miliary metastases from carcinoma of the kidney. Postmortem examination showed miliary distribution of tumor nodules throughout both lungs. The streak-like shadows extending out from the hilar areas were due to lymphatics filled with tumor cells. The hilar nodes were enlarged and invaded by the neoplasm.

pearance suggesting a primary cancer of the bronchus (Fig. 14). Predominantly pleural involvement was not often present; when seen, there was also usually an associated pleural effusion (Fig. 15).

Prostate. Cancer of the prostate gives rise to pulmonary metastases less frequently than hypernephroma. In a group of 22 cases, Kaufman[28] reported the lungs

FIG. 13. Metastases to mediastinal and hilar lymph nodes from carcinoma of the kidney. The appearance suggests lymphoblastoma. The postmortem examination also showed a few small tumor nodules at the right base.

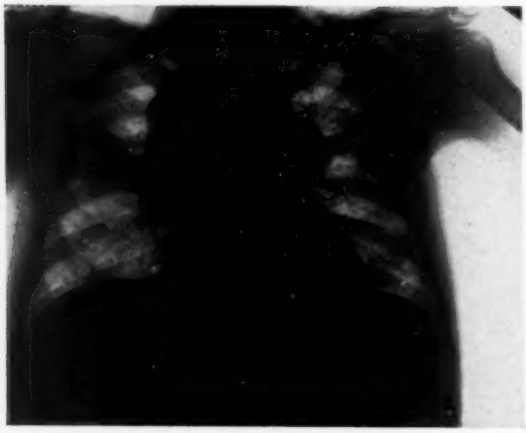


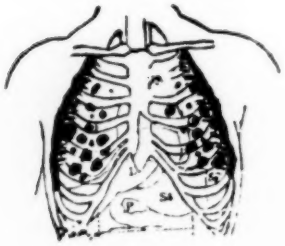
Fig. 14. Metastases to the lungs, mediastinal and hilar lymph nodes from carcinoma of the kidney. The appearance is suggestive of carcinoma of the lung. Postmortem examination showed neoplastic masses in both hilar regions. From these areas there radiated a series of small tumor nodules, particularly along the course of the bronchi and in the upper lobes.

Fig. 15. Pulmonary and pleural metastases from carcinoma of the kidney. Postmortem examination showed infiltration of the pleura of both lungs with carcinoma. The lymph vessels of the lungs, also the hilar nodes, were invaded by neoplasm.

CARCINOMA OF THE PROSTATE

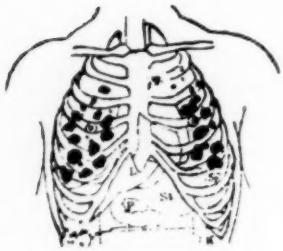
Pulmonary And Pleural Metastases.

Total Number Of Cases	60
Total Number Of Postmortems	39
Total Number Of Pul. or Pl. Met.	26 - 43% (20 Verified at P.M. (6 Diag. Only by X-ray.



Postmortem Findings In Lungs

1. Nodules in pleura and lungs most frequent.
2. Next in frequency, nodular parenchymal lesions, occasionally lymphangitic in type.
3. In a few cases, only hilar nodes were involved.
4. Pulmonary lymphatics were frequently invaded.



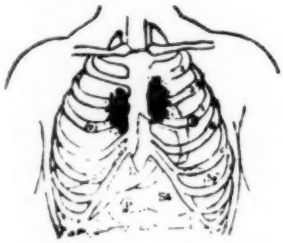


Fig. 16.

involved in 40 per cent and the pleura in 58 per cent. Willis[41] found pulmonary involvement in 35 per cent and Turner and Jaffe[39] in only 28.4 per cent of 95 autopsies.

In this group, 26 cases (43 per cent) had intrathoracic extension of the disease (Fig. 16). At postmortem, the most frequent finding was the association of pleural and pulmonary metastases. In these patients, the pleura was either studded with nodules or else diffusely infiltrated (Fig. 17). The pulmonary lesions consisted of subpleural infiltrations and nodules scattered throughout the lungs. Pleural effusions were common in this group. Next in frequency were parenchymal lesions, consisting either of numerous nodules, pea-sized to miliary, or else a few large circular masses. Rarely only a single nodule was found. At times, the involvement was predominantly hilar, with extension therefrom into the lower lobes of both lungs. Pleural lesions were also occasionally present with this type. In a few instances, the lungs appeared negative macroscopically but microscopic sections showed invasion by tumor cells of the parenchyma or peribronchial lymphatics.

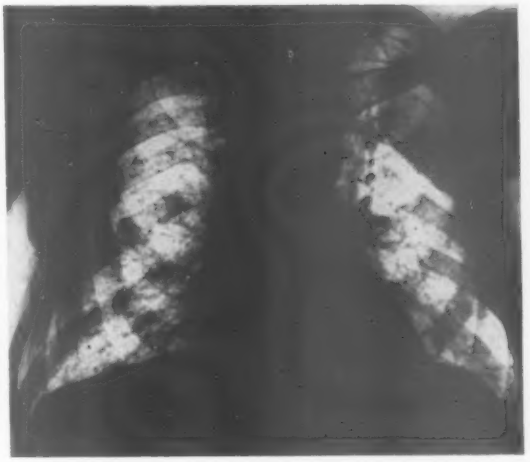


FIG. 17. Pleural metastasis from carcinoma of the prostate. The metastasis appears as a scalloped shadow along the periphery of the left pulmonary field (arrow). The left infraclavicular shadow is due to a rib metastasis.

CARCINOMA OF THE BLADDER

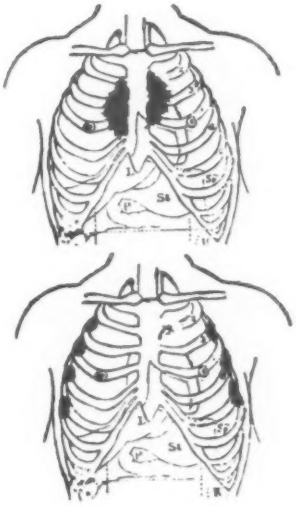
Pulmonary And Pleural Metastases.

Total Number Of Cases 56

Total Number of Postmortems 35

Total Number Of Cases With

Intrathoracic Involvement 4 - 7% (All Verified at P.M.)



Postmortem Findings In Chest

1. Metast. to mediast. glands in one patient.
2. Metast. to hilar nodes. Tumor cells in capillaries, veins and lymphatics.
3. Few small subpleural nodules in another patient.
4. Tumor cells found in one instance in a thrombus in an artery of the lung.

FIG. 18.

Bladder. The literature is most confusing on the frequency of pulmonary metastases from cancer of the bladder. Barringer[3] and Kaufman[28] state that such extensions are rare. Geraghty,[16] on the other hand, states that the lungs are a favorite site for these metastases. Spooner,[36] in his analysis previously referred to, reported pulmonary extension in 9 cases, or 5 per cent. The Carcinoma Registry of the American Urological Association[8] found 11 cases (14 per cent) of metastases to the lungs in 79 postmortem examinations. Turner and Jaffe[39] report 19.5 per cent involvement in 46 postmortems.

In this series, 4 cases, or 7 per cent, showed intrathoracic involvement (Fig. 18). Two patients had metastases to the mediastinal or hilar nodes, 1 patient presented a few small subpleural nodules and in the last case, tumor cells were found in a thrombus in an artery of the lung. In these patients, the tumor had extended outside the bladder to involve the regional glands.

Symptoms. Cough and dyspnea are the two complaints most commonly encountered when pulmonary involvement is present. Pain occurs next in frequency. Hemoptysis rarely presents itself as a symptom. In a small number of patients, physical signs, such as dullness, diminished breath sounds and râles, are the first indication of pulmonary metastases. If the pulmonary involvement is slight, no symptoms or physical signs may be present and the lesions are then discovered only on roentgen or postmortem examination.

When the predominant lesion is parenchymal, as in the case of hypernephroma, cough is the most frequent symptom. Where the pleura is most frequently involved, as in prostatic carcinoma, dyspnea due to pleural effusions, and pain are the earliest manifestations of the intrathoracic involvement.

Mode of Spread of Metastases. The kidney has a very rich vascular supply and early invasion of the blood stream by cancer is frequent. It is therefore to be expected that pulmonary metastases from kidney malignancies should be embolic by way of the blood stream. The predominance of parenchymal lesions bears this out. The postmortem material also shows that pulmonary involvement occurs by lymphatic permeation through the diaphragm and on to the parietal pleura, and by way of emboli along lymphatic channels.

The frequency of both pleural and parenchymal involvement from cancer of the prostate suggests invasion by both lymphatic and hematogenous routes. The prostate is richly supplied with lymphatics. Extension takes place by way of the regional nodes to the mesenteric and retroperitoneal nodes, thence to the thoracic nodes and then retrograde to the lung and pleura along the smaller lymphatics.

Effect of Radiotherapy. Irradiation is often ineffectual with pulmonary metastases from cancer of the urinary tract. Lung involvement is frequently a terminal affair and is usually associated with metastases to other viscera. The patients are in such poor general condition that they cannot tolerate the large doses of radiation necessary for relief of symptoms. Occasionally, however, relief of cough and dyspnea and, when pleural effusions are present, slower refilling of the chest will follow such treatment.

CONCLUSIONS

1. Skeletal and pulmonary metastases were investigated, either by roentgen or postmortem examinations, in 203 patients who died from cancer of the kidney, prostate and bladder.

2. Of 87 patients with cancer of the kidney, 39 cases, or 45 per cent, revealed skeletal metastases. In 47 instances, or 54 per cent, pulmonary, pleural or mediastinal metastases were also present.

3. Sixty patients with cancer of the prostate were investigated. In 35 cases, or 58 per cent, skeletal metastases were found. Pulmonary, pleural or mediastinal involvement was discovered in 26 cases, or 43 per cent.

4. Of 56 patients with cancer of the bladder, bone involvement was present in 6 cases, or 10 per cent, but in only one instance were true metastases observed. In the other cases, the pelvis was invaded by direct extension from the primary tumor. In this series, 4 cases, or 7 per cent, showed intrathoracic involvement.

5. Intensive radiotherapy relieves pain in a large number of patients with skeletal metastases from cancer of the kidney and prostate.

6. Irradiation is often ineffectual in pulmonary metastases from cancer of the urinary tract. Occasionally, however, relief of cough and dyspnea and, when pleural effusions are present, slower refilling of the chest will follow such treatment.

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Vol. 55, No. 2

ABDOMINAL LYMPHOGRANULOMATOSIS

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ALTHOUGH enlargement of the superficial lymph nodes is the most spectacular aspect of Hodgkin's disease and the most frequent reason for the patient to seek medical attention, other manifestations of the disease have been the subject of investigations in recent years. For example, lymphomatous involvement of the pulmonary[15] and osseous[16] systems and of the breast[1] have been studied intensively in the past few years at the Memorial Hospital. Since approximately 15 per cent of the cases of Hodgkin's disease seen at this institution develop symptoms referable to the gastrointestinal tract at some period of the illness, it was thought that a study of the abdominal manifestations of this malady might be instructive.

Terplan[14] divided cases of Hodgkin's disease of the gastrointestinal tract into those in which the digestive tract is exclusively involved and those in which it is involved as part of a generalized or disseminated process. This grouping does not include those cases in which there are gastrointestinal manifestations produced by extrinsic disease. Therefore the following classification is proposed.

1. Primary gastrointestinal lymphogranulomatosis.
2. Secondary gastrointestinal lymphogranulomatosis.
3. Extrinsic gastrointestinal lymphogranulomatosis.

The accurate differentiation of these three groups may sometimes be impossible by clinical means. In these instances the distinction can only be made by postmortem study.

PRIMARY LYMPHOGRANULOMATOSIS OF THE GASTROINTESTINAL TRACT

Attention to primary lymphogranulomatosis as a clinical entity was drawn by Schlagenhaufer[11] in 1913 when he described gastric lymphogranulomatosis without involvement of any other organ. Previous to this according to Terplan[14] the localized form of lymphogranulomatosis was probably classified as sarcoma of the bowel or tuberculous enteritis. By 1927 Hayden and Apfelbach[7] were able to collect 26 cases from the literature and to add 3 of their own. Singer,[12] in 1931, reviewed the literature and selected 6 cases which he concluded were unquestionable examples of primary gastric lymphogranulomatosis, in which no other focus of disease was demonstrable, and added 1 of his own. In 1936 Madding[8] of the Mayo Clinic published a report on 6 cases of primary Hodgkin's disease of the stomach which had been seen over a period of the preceding eight years. Bini and Parvis,[2] in 1940, published a paper on primary lymphogranulomatosis of the gastrointestinal tract in which they reviewed the literature exhaustively. There were over a hundred references cited which represented about 150 cases.

Primary lymphogranulomatosis may involve any part of the gastrointestinal tract or several segments concomitantly; the stomach, however, appears to be the most frequent site. The symptomatology is dependent upon the portion of the digestive tract involved. The majority of the patients are in the fifth decade and males predominate in the ratio of 2 to 1.

Lymphogranulomatosis of the stomach may involve any portion of the organ. The pylorus, however, is the most frequent site. The presenting symptoms may be epigastric or abdominal pain relieved in some instances by food or alkalies, postprandial distress, nausea, vomiting, gaseous eructations and anorexia. There may be weakness, loss of weight and hematemesis. The process may produce pyloric obstruction with

its concomitant signs and symptoms.

Gastric analysis may show an achlorhydria but in many instances the gastric acidity is within normal limits. There may be a moderate secondary anemia. There is usually no significant alteration in the leukocytes with the exception of an occasional slight eosinophilia.

Physical examination is for the most part non-contributory. There may occasionally be some evidence of weight loss. A palpable mass in the abdomen is uncommon and the liver and spleen are usually not felt. Superficial lymphadenopathy and pyrexia are infrequent.

Roentgen studies may reveal a filling defect which is interpreted as being caused by a cancer or ulcer. When the roentgenologic and physical findings are correlated with the symptomatology the diagnosis in nearly all instances is neoplasm or ulcer, the former being the more frequent conclusion. The correct diagnosis is made at operation or autopsy.

The lesions, which are grayish or pearly white in color, may occur in any part of the stomach. They may be flat, nodular, or in some instances in the form of convolutions somewhat resembling those of the cerebrum. Macroscopically the disease appears as an infiltration with consequent thickening of the gastric wall. It may be limited to a small area or it may be diffuse throughout the whole organ producing an effect similar to linitis plastica. The lesion may be ulcerated and bear a resemblance to a neoplasm. The ulceration may give rise to perforation or to hemorrhage which on occasion may be severe enough to cause death. The adjacent lymph nodes may be large, discrete, soft and succulent.

The treatment for disease localized to the stomach is gastric resection. Involved omental nodes should be removed at the same time. In some of the cases reported from the Mayo Clinic in which involved omental nodes were removed at the resection, the patients were alive and apparently free from disease six to eight years later.

The incidence of this disease in the intestine is greatest in the upper part of the small bowel and decreases from there to the rectum. Involvement of the bowel may be characterized by malaise, weakness, abdominal pain, meteorism, diarrhea, constipation or alternating diarrhea and constipation. There may be irregular bouts of fever and occasionally a palpable abdominal or rectal mass. Superficial lymphadenopathy is infrequent. Often there is a secondary anemia and sometimes a leukopenia. With this symptomatology the condition may simulate typhoid fever. On the other hand, the clinical picture may be that of an acute obstruction or intussusception. There may be perforation with peritonitis or hemorrhage which may be fatal. The diagnosis is established at laparotomy. Surgical removal of the lesion relieves the symptoms and in numerous instances has apparently effected a cure.

SECONDARY LYMPHOGRANULOMATOSIS OF THE GASTROINTESTINAL TRACT

Secondary lymphogranulomatosis of the gastrointestinal tract occurs as part of the generalized disease process. Pitt[10] in 1889 described lesions in the stomach and duodenum occurring under these circumstances. The patient may or may not complain of gastrointestinal symptoms and the lesion may be discovered only at postmortem examination. In a series of 295 deaths from Hodgkin's disease in cases followed at the Memorial Hospital during the decade of 1932 to 1942 there were 36 autopsies. Six, or 1.7 per cent, of these revealed, in association with the generalized disease, lesions of the gastrointestinal tract—5 in the stomach and 1 in the duodenum. The duodenal lesion was a healed ulcer whose base showed Hodgkin's disease on microscopic examination and it was assumed that the ulceration was secondary to the lymphogranulomatous process. This patient had gastric symptoms when first seen at the clinic. There was no ulcer history but a gastrointestinal roentgen examination was reported as suggestive of duodenal ulcer.

Of the 5 patients with gastric involve-

ment, 2 gave a history of epigastric pain, nausea and vomiting. In 1, a woman, roentgen studies revealed an irregularity in the prepyloric region where, at autopsy, a large superficial ulcer with slightly elevated edges was found. Microscopic examination revealed the ulcer to be, for the most part, nonspecific but to have minute specific lesions at its base. In the other patient, although the gastrointestinal series failed to reveal any abnormality, at autopsy a nodular excrescence was found in the fundus which was pronounced Hodgkin's disease on microscopic study. In addition, near the antrum, in an area free of Hodgkin's disease, was a punched out ulcer 3 cm. in diameter, which microscopically suggested an ulcerating cancer. It is of interest that the initial superficial lymph node in each of these cases appeared in the inguinal region and showed Hodgkin's disease on biopsy. In the 3 cases that had no gastric symptoms, nodular lesions, proved to be Hodgkin's disease by microscopic examination, were found at autopsy in the gastric wall. The sites of involvement were the pylorus, the posterior gastric wall and the greater curvature respectively. Thus it appears that intrinsic disease of the stomach may remain asymptomatic.

In another patient a diagnosis of secondary intrinsic disease of the stomach was established by gastroscopic examination.

This patient was an Italian woman, aged twenty-nine, who came to the clinic complaining of a swelling in the left side of the neck which appeared one year previously and had increased somewhat in size since its inception. Later she developed a dry non-productive cough. Examination was negative except for an indefinite swelling over the lower third of the left sternocleidomastoid muscle. Two small soft nodes were palpable near the swelling. A biopsy of one of these nodes was reported as Hodgkin's granuloma. A roentgenogram of the chest revealed a mediastinal mass displacing the trachea to the right. She received roentgen therapy to the left neck and mediastinum with marked regression of the lesions and she remained well, except for a small right supraclavicular node controlled by roentgen therapy, for a period of two and a half years. At this time she developed gastric distress and diarrhea. A gastrointestinal roentgen examination revealed a slight sawtooth appearance along the lesser curvature. A gastroscopy was performed at which a definite nodular and linear infiltration of the pars media and lesser curvature was seen as well as numerous punctate hemorrhages in the area of infiltration. The gastroscopist made a diagnosis of Hodgkin's disease involving the pars media of the stomach. High voltage roentgen therapy was administered to the stomach through an anterior and posterior field giving a dose of 1,200 r to each area. This was followed by a disappearance of the gastrointestinal symptoms, and at gastroscopy two months later no abnormality of the stomach was seen. With the exception of the appearance of a node in the right spinal accessory chain, the patient has remained well to date (five and a half years).

Secondary involvement of the gastrointestinal tract might be a more common occurrence if the individual did not succumb to the disease so early. The retroperitoneal nodes involved by this disease increase slowly in size over a long period of time and rarely demonstrate invasive characteristics. That this may occur, however, in the relatively long lived patient is illustrated by the following case:

This patient was a female, aged twenty-two, whose illness began in 1929 with enlargement of the left cervical lymph nodes followed by enlargement of those in the left axilla. An axillary and cervical node were removed at another institution and diagnosed as Hodgkin's disease following which she received five roentgen treatments to the neck and axilla over a period of seventeen months. She was then referred to the Memorial Hospital for further treatment. Examination in November, 1931, at this institution revealed enlarged nodes in the left neck, left supraclavicular region and in both axillae. In May, 1934, about five years after the onset of her illness, she began to develop severe pain in the right upper quadrant of the abdomen. No masses or organs were palpable. The pain subsided after several weeks and she remained asymptomatic for about one year.

In May, 1935, she returned with a complaint of severe upper abdominal pain which required sedatives for relief. Examination revealed a nodular mass in the left upper quadrant near

the midline which was interpreted as a group of lymph nodes. This area was irradiated, followed by subsidence of the mass and relief of the pain. However, the pain returned in a few months at which time a gastrointestinal roentgen examination was done and reported negative. Again there was a response of the pain to radiation therapy and an interval of freedom from discomfort.

For the next four years she had attacks of abdominal pain at intervals which were controlled by radiation therapy. During this period she also developed evidence of the disease in the mediastinum, lungs, pelvis and inguinal nodes and received roentgen therapy to these locations.

In 1941, twelve years after the onset of the disease, she developed lower abdominal cramps and diarrhea. Rectal examination revealed a firm, lobulated mass outside the rectal wall and posterior to it. Other masses were palpable throughout the lower abdomen. The intestinal symptoms continued as well as the abdominal pain and vomiting. Proctoscopic examination revealed a stenosis about 8 cm. up and grayish white thickened areas in this location. A biopsy of one of these lesions was diagnosed as Hodgkin's disease. A gastrointestinal series showed no evidence of intrinsic esophageal, gastric or duodenal disease. Radiation therapy was given to the rectal lesions but the patient's course was progressively retrogressive. She continued to have abdominal pain until her death a few months later. Her disease lasted thirteen years.

EXTRINSIC GASTROINTESTINAL LYMPHOGRANULOMATOSIS

In this group are the cases of Hodgkin's disease with gastrointestinal symptoms in which there is no clinical, roentgenographic or gastroscopic evidence of intrinsic gastrointestinal involvement but in which the symptoms are produced by extrinsic pressure of the enlarged abdominal lymph nodes. These are a continuation of the iliac chain and are divided into two groups: the mesenteric and the para-aortic. The nodes are connected by lymphatic vessels, the whole forming one closed system which empties into the left jugulosubclavian junction by means of the thoracic duct. The mesenteric nodes and lymph vessels follow the course of the blood vessels supplying the abdominal organs. The lymphatics of the small bowel, large bowel and rectum consist of chains of nodes and vessels which follow the course of the superior and inferior mesenteric blood vessels. The stomach is drained by lymphatic channels and nodes on the greater and lesser curvatures which accompany the gastric and gastroepiploic arteries respectively. The pancreas and spleen are supplied with lymphatic vessels and nodes which follow the course of the splenic artery. In like manner, the liver and gallbladder are drained by nodes and lymph channels which accompany the hepatic artery, portal vein, cystic and common ducts and right gastroepiploic artery.

The mesenteric system communicates with the para-aortic nodes (Fig. 1). These consist of twenty-five or thirty large nodes which are distributed along the abdominal aorta and inferior vena cava, and surround these vessels. Some of the nodes lie in front, some behind, others to the right and left of the great vessels. There are groups of nodes at the origin of the superior and inferior mesenteric arteries and of the celiac axis. The mesenteric system of lymphatics accompanying these trunks empties into these respective groups.

From 1932 to 1942 inclusive a group of 406 cases of Hodgkin's disease, proved by biopsy, was seen at the Memorial Hospital. At the time of writing 295 are dead and 111 living. Of the entire group 52, or 12.8 per cent, developed gastrointestinal symptoms. Seven of these cases, of which 6 revealed specific gastrointestinal lesions at autopsy and 1 by gastroscopy, have been discussed under a previous heading. Hence there were 45 patients, or 11 per cent, in whom there was no clinical or roentgenographic evidence of intrinsic gastrointestinal involvement.

These figures are smaller than those of other investigators. Ziegler,[17] for example, states that 35 per cent of the patients with Hodgkin's disease have gastrointestinal disturbances of which diarrhea is the most common symptom. Minot and Isaacs[9] analyzed 477 cases of lymphoblastoma and

found that 25 per cent had as their initial symptom one referable to an abdominal lesion. No attempt was made to break down the grouped lymphoblastoma into its component elements so that this figure is not comparable with the one we obtained for Hodgkin's disease.

The average age of the 52 patients developing gastrointestinal manifestations was thirty-six years. The number of males in this group was 39, or 75 per cent, and the number of females 13, or 25 per cent. These figures for average age and sex distribution correspond with those for Hodgkin's disease in general.

The initial complaint in 37 of the patients, or 71 per cent, was enlarged cervical lymph nodes. This figure is comparable with that given by Goldman[6] for Hodgkin's disease as a whole. The frequency with which the initial nodes occurred in the various sites is shown in Table 1.

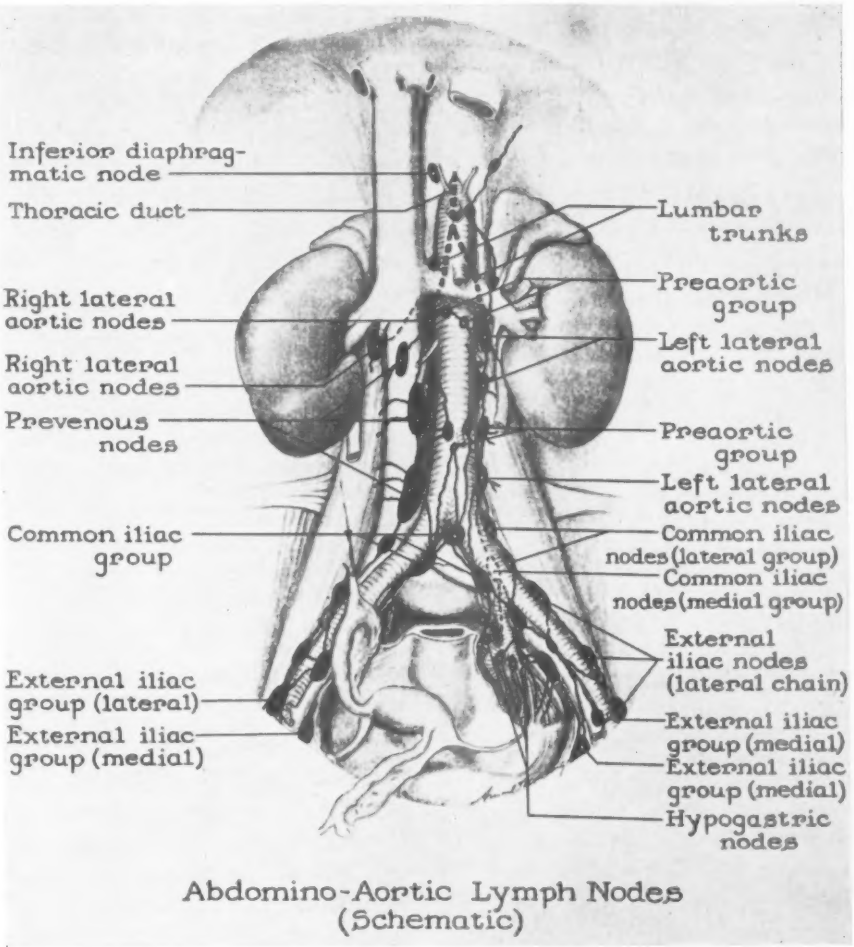

Fig. 1. Adapted from "Anatomy of the Human Lymphatic System" by Rouviére, translated by Tobias. Edwards Bros., Inc., Ann Arbor, Mich. 1938. (Reproduced by permission.)

The initial symptoms referable to the gastrointestinal tract were in most cases abdominal pain or epigastric distress. Some individuals, however, had diarrhea, vomiting or gastric hemorrhage as the first symptom. The frequency of the various initial gastrointestinal complaints is summarized in Table II.

Roentgen studies of the gastrointestinal tract were carried out in 33 patients, or 63

TABLE I

SITE OF INITIAL SUPERFICIAL NODES IN 52 CASES OF HODGKIN'S DISEASE WITH GASTROINTESTINAL MANIFESTATIONS

Left neck	14
Left lower neck	11
Right neck	12
Axilla	4
Left submaxillary region	1
Suprasternal notch	1
Inguinal region	2
Unknown	2
No initial nodes	5

per cent of the cases. Of this group approximately 50 per cent failed to reveal any abnormality. The positive roentgen findings are given in Table III.

The average interval from the onset of the disease to the appearance of the gastrointestinal symptoms was two years and two months. This length of time approximates the average life expectancy in this disease which, according to numerous authors, is about two years and eight months.

The patients who developed gastrointestinal symptoms had an average life expectancy of three years and ten months, or one year and two months greater than the average life expectancy for all cases of Hodgkin's disease. Minot and Isaacs, in their analysis of a large group of lymphomas, also concluded that the duration of life was longer in those with symptoms referable to the gastrointestinal tract. On the other hand, we found that if the onset of the disease was with gastrointestinal manifestations then the life expectancy was short. The average duration of life in 6 patients of this category was nine and a half months.

TABLE II

INITIAL ABDOMINAL SYMPTOMS IN 52 CASES OF HODGKIN'S DISEASE WITH ABDOMINAL MANIFESTATIONS

Abdominal pain	19
Epigastric distress	16
Nausea and vomiting	5
Diarrhea	5
Dysphagia	3
Gastric hemorrhage	2
Flatulence	2

The explanation for the first phenomenon is probably that the patients who live longer develop the gastrointestinal complications. It is thought by some students of the subject (Symmers,[13] Ewing,[4] Desjardins[3]) that the retroperitoneal lymph nodes are involved early in the disease but fail to produce symptoms because, as they increase slowly in size, the abdominal organs are able to adjust to this growth for a long period of time. It is only when the viscera can no longer accommodate themselves to the enlargement of the masses that pressure symptoms arise. Hence these symptoms are a late manifestation and only those patients who live long enough develop them. The superficial, especially the cervical lymphadenopathy is but an external manifestation of this involvement. The finding that 37 out of 52 cases (71 per cent) in the present series had the original nodes in the neck tends to support this view.

TABLE III

POSITIVE ROENTGEN FINDINGS IN 14 CASES WITH ABDOMINAL LYMPHOGRANULOMATOSIS

Displacement of stomach or duodenum due to extragastric mass	2
Ulcer at the cardia	1
Deformity of lesser curvature	2
Irregularity of prepyloric region	1
Crater of the duodenal bulb (ulcer history)	2
Irregularity of duodenum	4
Pyloric defect	1
Narrowing of descending colon	1

A case that illustrates the relationship between cervical and retroperitoneal disease is the following:

The patient, a male, aged fifty-six, came to the clinic with the complaint of a hard swelling in the right side of the neck of three months' duration. Examination revealed several firm nodes on the right side of the neck, one of which was biopsied and reported as Hodgkin's disease. There were no other evidences of disease and a roentgenogram of the chest was negative. On the basis of these findings the case was thought suitable for surgery so a radical neck dissection

was performed, followed by deep roentgen therapy to the area. Within a year the patient developed epigastric distress, an abdominal mass and right supraclavicular and axillary nodes. A gastrointestinal examination showed displacement of the stomach probably due to upper abdominal disease. The patient succumbed less than one year later.

In those cases in which the initial symptom is referable to the gastrointestinal tract and the duration of life thereafter is short, intra-abdominal disease has probably been present for a considerable period although the patient may have been relatively asymptomatic and may have had no discernible external lymph node involvement. He may have had vague abdominal pains or aches, especially backache, for months without its significance being appreciated. When the gastrointestinal symptoms ultimately appear the patient is already in the terminal stage of the disease.

That Hodgkin's disease may be confined to the abdomen for a long period of time without external manifestations is illustrated by the following case:

The patient was a female, aged twenty-nine, whose initial symptom was weakness following the birth of her second baby. She developed a secondary anemia and progressive weakness over a period of eighteen months. Then she developed a lumbar backache and shortly thereafter a tumor was found in the left upper quadrant of the abdomen. There was no external lymphadenopathy. An abdominal exploration was performed at which a large retroperitoneal mass was found above the lesser curvature of the stomach. In the gastrohepatic omentum there was a mass of nodes which involved the stomach and there were numerous enlarged nodes along the greater curvature. One of these was removed and reported as cellular Hodgkin's disease.

The mass completely disappeared following high voltage roentgen irradiation and the patient was asymptomatic for four years. There was at no time any demonstrable superficial lymphadenopathy. One year later, or five years after the onset of the illness, a mass began to develop in the epigastrium associated with nausea and vomiting. Despite irradiation the condition grew worse until there was complete pyloric obstruction. A gastroenterostomy was performed. The pyloric end of the stomach was involved in a mass which completely surrounded it. No enlarged nodes were found either in the gastrocolic or gastrohepatic omentum. She died three months later.

Enlargement of the retroperitoneal nodes may be accompanied by pyrexia. For this reason a diagnosis of appendicitis is occasionally made when the pressure produces right lower quadrant pain associated with fever. There were 3 such patients in this series. Two were subjected to laparotomy before coming to this clinic and the third refused operation despite the fact that his physician made a diagnosis of ruptured appendix with peritonitis.

Jaundice may occur in this disease due to pressure on the extrahepatic ducts by enlarged nodes or to pressure on the intralobular ducts by intrinsic liver disease. There were 4 jaundiced patients in this series.

Therapy is dependent upon the group in which the disease falls. In primary lymphogranulomatosis of the gastrointestinal tract the procedure of choice is surgery, even though the regional nodes may be involved. These gastric cases are usually explored because of a diagnosis of carcinoma. Gastroscopy should afford a means of making the correct preoperative diagnosis in some of these individuals. Gall[5] has recently published statistics which show that cases of lymphoma which can be treated surgically have twice the life expectancy of those treated by other methods.

With secondary involvement and with extrinsic gastrointestinal disease the treatment is symptomatic. In addition to transfusion and general supportive measures the chief therapeutic agent is roentgen radiation. The superficial nodes as well as mediastinal masses are irradiated as they appear. The abdomen is irradiated for pain, epigastric distress, nausea, vomiting or diarrhea with excellent palliation. Attacks of pyrexia are also controlled by irradiating the retroperitoneal lymph nodes even though they may not be palpable. Many

patients are relieved of their symptoms for a longer or shorter period of time. This form of therapy does not increase the life expectancy but it does keep the patient comfortable and allows him to carry on for many months or several years in some instances.

SUMMARY AND CONCLUSIONS

1. There were symptoms referable to the gastrointestinal tract in 13 per cent of 406 cases of Hodgkin's disease studied at the Memorial Hospital from 1932 to 1942.

2. These symptoms may be produced by primary, secondary or extrinsic disease of the gastrointestinal tract.

3. Primary Hodgkin's disease of the gastrointestinal tract is a distinct entity whose treatment is surgical.

4. Secondary involvement of the gastrointestinal tract may be asymptomatic and discovered only at autopsy.

5. Gastrointestinal manifestations from secondary involvement or extrinsic Hodgkin's disease are usually a late occurrence and are found most frequently in the long lived patients.

6. If gastrointestinal symptoms appear early in the course of a generalized Hodgkin's disease the life expectancy as a rule is exceedingly short.

7. The clinical picture in some instances may resemble that of appendicitis.

8. Roentgen therapy may give considerable symptomatic relief in the cases of secondary or extrinsic Hodgkin's disease of the gastrointestinal tract but there is no evidence that the life expectancy is increased.

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Vol. 55, No. 2

PRIMARY MESOTHELIOMA (ENDOTHELIOMA) OF THE PLEURA

CASE REPORT

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WITHIN the past few years considerable literature has appeared on the subject of primary mesothelioma of the pleura. The varied nomenclature reflects the complexity of classifying primary diffuse pleural tumors. According to one group of writers,[15] nearly two hundred authors have discussed and offered opinions on this entity describing the perplexities of the clinical, roentgenographic and pathologic phases. The clinicians and roentgenologists indeed have a difficult diagnostic problem when the pathologists, with a section of tissue under the microscope, argue among themselves as to type and histologic origin of the neoplasm.

Reviewing numerous statistics and data, Saccone and Coblenz[15] concluded that the average frequency of this malignancy in necropsies is approximately 1.1 cases per thousand. The age distribution showed the greatest prevalence in the forty to sixty year bracket. Birnbaum[3] stated that a predominance of the tumor in males existed in a ratio of about 2 to 1. There seems to be little difference in predilection of the pleural cancer for either right or left side of the thorax.

The clinical findings are quite variable and confusing, simulating the effects of a chronic inflammatory process and thereby masking the true malignant factor. Certain symptoms, nevertheless, predominate and are outstanding. Pain is persistent and appears early in the onset of the disease. A dry, irritating, non-productive cough soon appears. Hemoptysis is the unusual rather than the usual occurrence. Some dyspnea may be present and occasionally a low grade fever may exist. A rapid loss in energy and some loss in weight usually causes the patient to seek medical attention. Frequent respiratory affections are one of the major complaints of the patient.

Roentgen examination provides only little help in the early stages of the disease in attempting to identify the entity. A slight pleural effusion may be seen at the base of the involved lung. Later, the effusion becomes massive with obscuration of the entire lung field. Occasionally, tumor nodules can be demonstrated as in this case, but as a rule they are difficult to visualize. Doub and Jones[4] advocate instillation of air following aspiration of the fluid in order to outline the tumor nodules and they state that "in few conditions is it of more value." A roentgen kymographic study may be of aid in differentiating a cardiac tumor from a pleural one, if the latter is in close relation to the cardiac silhouette.

Significantly, in performing a thoracentesis for the pleural effusion, the needle seems to strike a solid resistant tissue with difficulty in forcing the needle through the thickened pleura. This fact has been emphasized by several authors[3,5,10,15] as a diagnostic aid. The pleural exudate may vary from a straw color, thin serous transudate to one of a hemorrhagic nature. Malignant cells may sometimes be found in the aspirated fluid but this finding is not pathognomonic of primary pleural cancer. DuBray and Rosson[5] state that "cytodiagnosis is of limited value in the clinical diagnosis of malignant pleural disease." Saccone and Coblenz[15] mention that a rapid reaccumulation of fluid occurs usually in a week or less following aspiration.

At necropsy, the macroscopic pathology presented is almost characteristic for this neoplasm. The pleura is irregularly thickened with firm, whitish, fibrous nodules

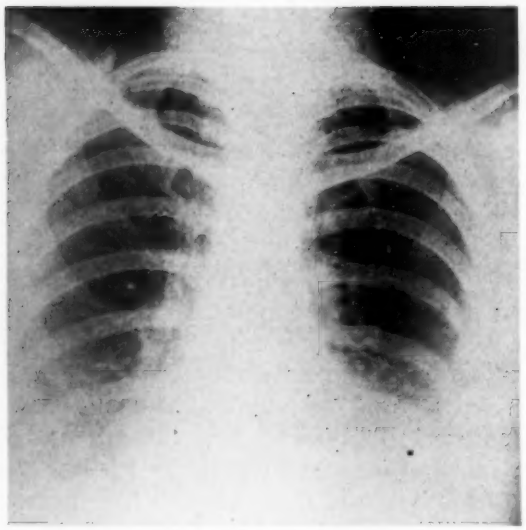

FIG. 1. The serofibrinous pleurisy at the left base of the lung can be visualized. No fracture of the ribs was discerned.

observed on the surface. The nodulations are conglomerate and diffuse, tending to encapsulate the lung and partially compress the lung parenchyma. Adhesions may fuse the layers of the pleura with often adherence of the pericardial sac to the malignant infiltration. Metastases are not common to distant organs, although cases have been reported with involvement in the kidney, spleen, adrenals, thyroid and brain. Metastatic bone invasion sometimes occurs in the ribs, and in our case the pelvis contained an extensive tumorous infiltration. There is wide extension in the majority of cases to all the surrounding areas and to the regional lymph nodes.

The microscopic picture reveals a prevalence of a fibrous stroma and the desmoplastic factor has been strongly emphasized by most writers. The tumor cells are of medium size, usually polyhedral, cuboidal or flat, and typically epithelial in appearance. These may appear as small alveoli, tubules, columns or nests. The nuclei are large, anaplastic and vesicular and very hyperchromatic, often showing pyknosis. Nucleoli are present in the cells and are usually faint. Lymphocytic infiltration may be seen in the pleural structure with evidence of chronic inflammation.

It is generally agreed that the pleura is derived embryologically from the mesoderm. However, controversy over the issue of the origin of pleural mesothelioma has resulted in several different views. The theory that the tumor arises from the endothelial lining of the pleura exclusively has the most support and adherents.[12,15,18] Ewing[6] and others[1,8] advance the view that the pleural endothelium or the endothelial cells of the lymphatic vessels of the subpleural space are the site of origin for the new growth. Another theory[9,11] strongly supported for a number of years was that the neoplasm originated only from the lymphatic endothelium of the pleura. Still others[14,19] express the opinion that there is no such thing as a primary pleural cancer and that it is secondary to malignancy elsewhere, such as primary bronchogenic carcinoma. One group[7,16] favors a hypothetical origin from aberrant nests of lung epithelium.

CASE REPORT

J.H.S., white female, aged thirty-three, in November, 1937, first visited a physician

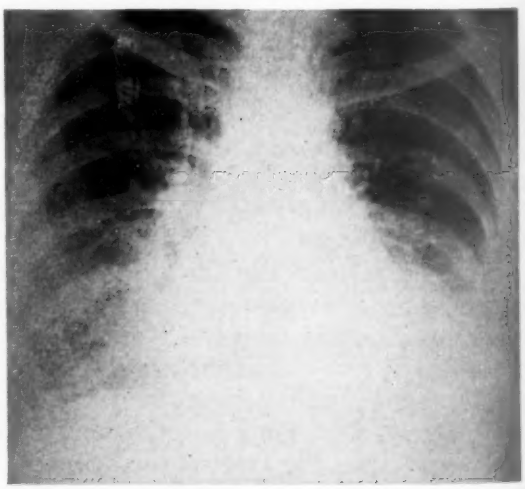

FIG. 2. The cardiac silhouette is increased as compared with the examination fifteen months previously. The pleural exudate has become quite prominent with obscuration of the left costophrenic angle, and the left diaphragm is elevated and partially fixed. (An artefact can be seen in the right upper lung field.)

(Dr. F.L.U.) with the complaint of constant pain in her left lower anterior thorax. A dry, unproductive cough was present and the patient stated that intermittently she had a low grade fever. She related that she suffered a fall in 1936, striking her left thorax with her elbow. From that time on she noticed some pain on moderate respiratory effort. Shortly after the accident, she had an attack of influenza and was confined to bed for ten days. She resumed work as a dictaphone operator but soon gave up her job as a result of continual tiredness and loss of energy. The patient thought that she had a persistent fractured rib due to the accident.

Her past history was essentially negative except for an appendectomy and salpingectomy many years ago, and the removal of her tonsils. She had had the usual childhood diseases.

Physical examination revealed a rather well nourished white female in her early thirties, not appearing acutely ill, weighing 149 pounds. Temperature was 99.2°F., with a normal pulse and respiration. Head and neck were essentially negative, except for moderate dental caries. No tonsils were present. Auscultation of the heart disclosed no abnormality with no enlargement on percussion. Blood pressure 122/78. Localized tenderness over the eighth left rib anteriorly in the axillary line was found; however, no crepitus was obtained. The breast sounds were of the bronchovesicular type with no râles audible in either lung field. The abdomen showed a midline scar below the umbilicus; there were no palpable masses.

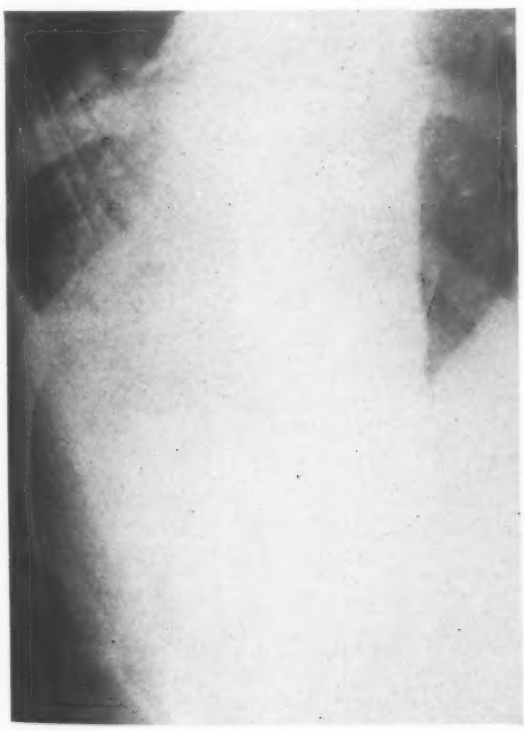

Fig. 3. A vertical fracture of the eighth left rib anteriorly is seen and appears of recent occurrence.

Fig. 4. A non-pulsating dense mass is noted in close relation to the left heart posteriorly and appears contiguous with the heart. Left oblique position.

A roentgenogram was made of the thorax on November 9, 1937, with the following report: "The cardiac shadow appeared normal in size and shape. The left diaphragm was flattened with what appears to be a serofibrinous pleurisy over the left diaphragm. A limitation of motion and excursion of the left diaphragm could be seen fluoroscopically. No evidence of a fractured rib could be ascertained." The left thorax was strapped for a week. After this, the patient was not seen again for fifteen months.

The patient was next seen on February 6, 1939, by the same physician (Dr. F.L.U.), complaining of the severe constant pain in her left chest of varying intensity with soreness now in

Fig. 5. Multiple osteolytic areas are observed in the bones of the pelvis after the administration of pitressin.

the small of her back. Dyspnea was quite pronounced on slight exertion and her husband remarked that when she slept a rather loud gurgling noise was evidenced during the respiratory phase. Loss in weight and protracted tiredness now were outstanding symptoms, as well as the dry cough.

Examination now showed a female with an early cachexia prevailing, weight 133 pounds. Temperature 99.4°F., pulse 92 and respiratory rate 22. Positive findings consisted of marked flatness over the left lower thorax posteriorly with subcrepitant râles on auscultation at the left base. Breath sounds in the left lung were bronchial in character. Respiratory motion on the left was limited. Tenderness was again localized over the eighth rib on the left side in the anterior axillary line. Auscultation of the heart revealed the muscular and valvular sounds to be within normal limits except for a tachycardia. Blood pressure 126/74. The remainder of the physical findings were normal. Laboratory findings were not unusual and were within the normal limits.

A roentgen examination of the chest was made on February 14, 1939. The following findings were reported: "Vertical fracture of the eighth rib on the left side somewhat anteriorly. The cardiac silhouette is considerably enlarged both to the right and left as compared with the previous exposure taken fifteen months ago, with a straightening of the left heart border. There is an obscuration of the left lower lung field as the result of pleural exudate with an eventration of the left diaphragm as evidenced under fluoroscopy. Considerable hilar and central root branch thickening is observed on both sides extending towards the bases. Thickening of the right upper interlobar septum was noted."

In view of the roentgenographic findings, the patient was referred to a cardiologist (Dr. R.C.P.) for consultation. His findings were essentially negative except for a sino-auricular tachycardia evidenced on the electrocardiogram. The increase in the cardiac dimensions were confirmed, as well as the pleural effusion at the left base. Palliative therapy was given for the pain in the way of mild analgesic medication and the patient was requested to return in a few weeks for another roentgen examination of the chest.

On March 31, 1939, a roentgen kymogram of the chest was made with the following findings: "The marked cardiac enlargement is as previously reported, more marked on the left. What appears to be a pleural exudate is observed at the left base behind the cardiac shadow and extending slightly up the lateral thoracic wall apparently due to capillary attraction. A dense mass about the size of a small egg is seen roentgenoscopically and kymographically in the left oblique position arising from the region of the lower left heart silhouette and in close relation to the cardiac shadow with a shifting of positions. There did not appear to be any definite pulsation of the tumefaction apparently

Fig. 6. The pleural effusion, fluid level and partial left pneumothorax are quite evident. The metastatic nodules in the right lung are of diffuse distribution.

arising from the left ventricle or pericardium at this site." A tentative diagnosis of a bronchogenic cancer was made with several other possibilities suggested, such as a rare cardiac neoplasm. Pleural mesothelioma was mentioned as a remote possibility.

Shortly after this the patient began to complain of pain in the pelvic region and lumbosacral spine. The pelvis was roentgenographed on May 5, 1939, following the administration of 1 cc. of pitressin intramuscularly, and the following findings were noted: "Several zones of radioparency in the region of the right iliac crest at the outer margin and near the left anterior inferior iliac spine could be discerned, as well as in the area of the right sacroiliac synchondrosis. The entire picture presents one of metastatic infiltration from a malignant growth." It was then felt that we were dealing with a primary pulmonary carcinoma secondarily involving the pericardium and pleura, with metastases to the rib and pelvis.

Palliative radiation therapy was administered to the thorax and pelvis for the agonizing constant pain. The factors were: 200 kv. constant potential; filtration 0.5 mm. copper plus 1.0 mm. aluminum in addition to the inherent filtration of 0.25 mm. copper; target-skin distance 50 cm.; 15 ma.; half-value layer 1.1 mm. copper. The pulmonary fields were confined to the left thorax and were three in number. The anterior and posterior fields were 15 by 15 cm. and the lateral field was 10 by 10 cm. The dosage was 200 roentgens (measured on the skin) given daily to one of the three fields, alternating the fields so that each one was treated every fourth day. The total dose delivered to each field was 2,000 r. Four pelvic fields were used, each 15 by 15 cm. (left and right anterior and posterior). A daily dose of 200 r was given to one field until a total dose of 1,000 r was administered to each of the four fields. Slight relief from the intense pain in the pelvis was observed after several treatments, but this was transient. A complete blood count was made near the termination of the course of irradiation, with the blood picture found to be within normal limits.

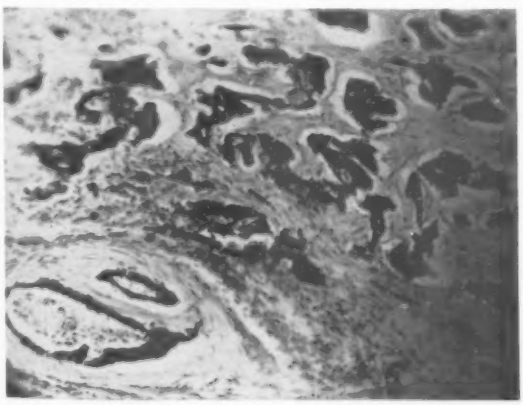

Fig. 7. Photomicrograph of left pleura (×80). Hematoxylin-eosin stain. Note the plexiform cords of tumor cells. The neoplastic cells can be seen lying in the lymph spaces as well as lining the lymph channels.

Fig. 8. Photograph of gross specimen of heart and lungs. The heart can be seen in the center of the specimen with the right lung uncompressed, and tumor nodules can be noted at the base. The left lung is markedly compressed and atelectatic, and is situated towards the rear of the specimen.

Shortly after irradiation was begun thoracentesis was performed to increase the effect of the roentgen therapy. The first was done on May 15, 1939, and 1,000 cc. of clear straw-colored fluid was aspirated. Some difficulty was noted in forcing the aspirating needle into the pleural space. This was casually mentioned and failed to impress us as a diagnostic feature. Aspiration was continued about every two weeks for four occasions and the exudate was serous and of a clear, amber color. Thoracentesis was always difficult to accomplish. No malignant cells were found microscopically in the aspirated fluid.

Roentgen therapy was limited due to acute respiratory embarrassment. A roentgenogram of the chest was taken soon after the completion of the roentgen treatments, on July 7, 1939. "A pleural effusion in the left lung with a fluid

level was discerned. A left partial pneumothorax is also noted. The right lung shows a diffuse mottled infiltration throughout and is probably metastatic invasion from the primary neoplasm. The enlargement of the cardiac silhouette is primarily to the left and may be due to pericardial sac retraction or effusion."

Later, the patient decided to go to Louisiana to visit her family. She remained there for approximately two months and while there was "tapped" twice and also given neoprontosil by mouth. She returned the first part of September, 1939, for observation and further care. Aspiration was again performed on September 10, 1939, and the fluid obtained was clear, bright red but did not have the viscosity of blood. Two more aspirations at ten day intervals were done, frank blood being obtained each time.

Dyspnea became quite pronounced and death ensued, typical of respiratory failure, on October 5, 1939. Just before death, she complained of severe pain of marked intensity in the pelvic region.

Autopsy. This was performed by Dr. Leo Lowbeer of Hillcrest Memorial Hospital, Tulsa, Oklahoma, on October 5, 1939. *Gross macroscopic examination* revealed a highly emaciated and anemic white woman with no evidence of cyanosis, edema or jaundice. The chest contained approximately 2,000 cc. of serous amber fluid in the right pleural cavity with no pleural adhesions noted. The right parietal and visceral pleurae were not thickened, although small tumor nodules were scattered throughout the entire surface of the pulmonary component. The left visceral pleura was firmly adherent to the pericardium on one side and to the parietal pleura of the upper lobe on the other side. An encapsulated exudate of about 1,000 cc. of rather cloudy, bloody fluid was found between the thickened layers of the visceral and parietal pleurae of the lower lobe. Almost the entire left visceral and parietal pleurae were altered, having a whitish appearance and being greatly thickened with adherence of the layers of the pleurae to each other as in the upper portion of the thorax, or forming pockets or sacs containing masses of fibrin, blood clots or serous fluid as in the lower thorax. The contiguous surfaces of the thickened pleurae presented numerous small whitish nodules. The entire left lung, especially the lower lobe, was small, compressed and atelectatic. On cut section, several small white nodules were found in the lung. The right lung showed some compression with numerous nodules scattered in both the upper and lower lobes. The large and small bronchi did not reveal any tumor arising from the mucosae of the bronchi. The mediastinal lymph nodes were infiltrated by the firm whitish tumor metastases.

The pericardial cavity was distended and also filled with fluid. The inner surface of the pericardial sac was covered with whitish gray neoplastic nodulations apparently penetrating from the adherent left visceral pleura. The heart was not enlarged, and did not show any pathologic change. The valves were normal and unaltered.

The eighth left rib was the seat of a cherry-sized osteoclastic metastasis.

Both breasts were normal, with no malignant infiltration.

An old incision in the midline of the lower abdomen was noted. Permission was not granted for examination of the abdominal contents; however, the abdominal cavity was inspected through the thoracic incision. The liver, spleen, kidneys, peritoneum and pelvic organs revealed no evidence of involvement by the neoplasm. Adhesions were observed in the pelvis with an absence of both uterine salpinges.

Microscopic examination revealed the left pleura to be enormously thickened, consisting of a fibrous stroma containing numerous, often densely packed alveoli, tubules, columns, nests and sheets of tumor cells. The cells were polyhedral or cuboidal in appearance, resembling epithelial cells with large anaplastic, pleomorphic, mostly round, very hyperchromatic, or even pyknotic nuclei. Solid nests and columns of these malignant cells could be seen filling and distending the countless lymph spaces all over the pleura. In some areas, an alveolar arrangement of the neoplastic cells occurred, while in others they seemed to line the lymph vessels. Occasionally, a solid plexiform structure of cells was observed with pearl-like formations resembling squamous cell carcinoma. The formation of lumina was discerned in some of the solid nests of tumor cells. Mitotic figures and some tumor giant cells were noted. The pleura showed evidence of chronic inflammation with lymphocytic infiltration. On the visceral surface, the pleura was covered with a thick layer of fibrin. The diaphragm did not reveal any tumor invasion.

The histopathological structure of the lung

metastases resembled that described in the primary pleural tumor, with the malignant cells frequently replacing the alveolar epithelium and lining the lung alveoli. The lumina of these alveolar structures often remained or were filled by masses of tumor cells.

The mediastinal lymph nodes contained metastatic cells forming solid alveoli and bands embedded in old hyaline fibrous scar tissue enclosing considerable anthracotic pigment. The cells were often arranged to form a lumen with the cells flattened in single rows simulating lymph spaces.

Pathologic Diagnosis: (1) primary mesothelioma (endothelioma) of the left pleura with an old encapsulated pleural serofibrinous-hemorrhagic exudate; (2) complete compression atelectasis of the left lung; (3) metastases to the pericardium with serofibrinous pericarditis; (4) metastases to the right visceral pleura with serofibrinous pleurisy; (5) metastases to both lungs especially the right; (6) metastases to the mediastinal lymph nodes; (7) osteoclastic metastases in the eighth left rib and pelvis.

COMMENT

The relative infrequency of this tumor, as well as the confusing clinical and roentgenologic features, has led us to submit a report of this case. The early symptom of constant pain with loss in energy, plus the persistent pleural effusion and difficulty in aspiration, should have made us strongly suspect the presence of a malignant pleural neoplasm in view of the roentgenographic findings. The increasing diameter of the cardiac silhouette to the left suggested a heart disease in spite of the lack of other cardiac confirmatory evidence and confused the diagnosis. The roentgen kymographic study indicated a non-pulsating tumor but the contiguity with the heart shadow made it appear that we might be dealing with a rare cardiac neoplasm. It is interesting to note the duration of the symptoms. For over a period of two years the patient had the intense gnawing pain in her left lower thorax, interpreting it as the result of an injury sustained to this region. Undoubtedly the rib invasion was in close conjunction with the onset of the disease. The rib fracture had the appearance of a recent one, with no roentgen signs of a metastatic process, either osteoclastic or osteoplastic. The history of a single acute trauma again brings up the much discussed point as to what part trauma[13] did play in the disease. It is believed that the blow to the thorax was coincidental, although it is quite possible that it may have prepared the site for the metastasis by lowering rib resistance (localized hemorrhage and interference with circulation).

The question arises as to what effect radiation therapy has on this type of neoplasm. The mere presence of anaplastic cells together with their debatable histologic origin alone does not indicate that this new growth is radiosensitive in that the desmoplastic matrix of the mesothelial cellular elements would tend to negate these factors. Little definite irradiation effect could be ascertained in the microscopic findings. To a slight degree, the hyperchromatism, pyknosis, lymphocytic infiltration and fibrous connective tissue stroma may have resulted from irradiation but this is to be questioned in that the same changes have been described by various authors[12,15] in untreated cases. Possibly dosage was inadequate since the therapy was terminated on the thorax after a total of 6,000 r on the skin because of the patient's respiratory discomfort. A tumor dose could not be determined with any degree of accuracy on account of the persistent pleural effusion and the diffuseness of the lesion. The obstructive phenomena in the lymph channels by tumor cells observed microscopically may have interfered with the cell-fluid exchange increasing the effusion in the left chest cavity. Stewart and Farrow[17] mention that one case of pleural endothelioma, treated by radiation therapy, showed no response after a dosage of 6,000 r. Others[10,18] have mentioned the use of roentgen therapy as a palliative measure with temporary improvement clinically. The doses have varied from 5,000 to 6,000 r, with no reference as to whether these were tumor or

skin doses. Microscopic alteration or influence on the tumor following irradiation has not been previously alluded to and it is to be wondered to what extent irradiation influenced the neoplasm to bring about improvement, if any.

The next question is whether or not irradiation increased the atelectatic and fibrosing processes in the left lung. Only speculation can be made in an attempt to answer this question. If the mesothelial cells were not affected, then one could hardly expect the fibrous connective tissue to be influenced, and stroma of this type could occur only as the end-result of intense irradiation. Nevertheless, it must be kept in mind that a stimulating dose might have been given the neoplasm. The value of roentgen therapy in this condition is difficult to determine, and more histopathologic studies should be made in order to properly interpret its efficacy.

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The author wishes to thank Dr. F. L. Underwood and Dr. Leo Lowbeer, of Tulsa, Oklahoma, for their cooperation and permission to report this case.

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Vol. 55, No. 2

UNUSUAL URINARY CALCULI

BRIEF REVIEW OF THE LITERATURE AND REPORT OF SIX CASES*

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IN JULY, 1896, only six months after Röntgen discovered the x-ray, James Adams, a Glasgow Surgeon, first detected roentgenographically and successfully removed a renal calculus. Usually, one can recognize a calculus from the plain roentgenogram, but in many cases excretory or retrograde pyelography or both are necessary for exact diagnosis and localization.

This discussion will be limited to a few of the more interesting recorded cases and a report of our 6 unusual cases of urinary calculi selected from patients studied at the Misericordia Hospital during the past seventeen years. The diagnosis of these cases could be easily made from the plain roentgenogram alone; and the calculi are of unusual interest because of their size, location and history of development.

Since the introduction of intravenous urography by von Lichtenberg and Swick[43] in 1929 the literature on urinary tract disease has greatly increased, and it has been estimated that about 80 per cent of urinary tract studies have been made for the determination of the presence or absence of urinary calculi.

REVIEW OF THE LITERATURE

Caulk[7] reported giant coral stones which completely filled the pelvis and calices of both kidneys. The right calculus measured 12 cm. and the left 16.5 cm. in their vertical diameters. There was also a bladder stone 8.5 cm. in diameter.

Harries,[19] in 1937 described a case of bilateral renal calculi in a male, aged fifty-two, in which the right kidney stone weighed 24 ounces and the left 9 ounces. The chief complaint was a lump in the right side which appeared nine months previous to his admission to the hospital.

Cecil[8] reported a hollow right renal stone 3.5 by 3 by 2 cm. in a male, aged thirty-one. The patient was kicked by a horse at the age of three, and the lower right ribs were fractured.

Stevens[39] reported a case of bilateral giant ureteral calculi in a male, aged thirty-three. The left weighed 50 grams, the right 18 grams.

Randall[35] described the largest bladder stone on record; it measured 48 cm. in its greatest circumference and weighed 64 ounces wet and 56 ounces when dry.

Holman[24] reported a urethral stone in an eight and one-half months pregnant woman. Several months before, she attempted abortion with slippery elm. A piece of elm bark was found as the nucleus. The stone measured $2\frac{1}{8}$ by $1\frac{1}{4}$ inches in diameter.

In 1943, Higgins[22] of the Cleveland Clinic reported 7 cases of urethral stones in a twenty-two year period after 1921.

Graham[18] described the case of a male, aged fifty-two, with pain and swelling in the perineum. In 1930, the patient was kicked between the legs. For the next two weeks he had occasional hematuria; later a perineal abscess developed which left a draining sinus. In 1938 he developed acute retention and a lump the size of a hen's egg, in the perineum. The removed calculus from the posterior urethra weighed 24 grams.

LeComte[29] noted that calculi seldom lodge in the male urethra. He found only 7 instances in 2,900 urological cases. He also mentions a case in which 230 stones were passed.

Brooksher[5] reports the case of a male, aged forty, who, two years before study, had a series of right renal colic and passed four stones one year later. He was symptom free for one year, then he had difficulty in voiding. By manipulation with the scope a stone was passed from the urethra.

Englisch[15] observed that about 42 per cent of urethral calculi are in the membranous portion and 48 per cent in the anterior portion of the urethra.

Joly[26] noted that 18 per cent of urethral calculi are associated with calculi elsewhere in the urinary tract.

Up to 1943, Lane[28] found 39 cases of urethral calculi in the literature and added 1 of his own.

Debenham[9] recorded 40 cases of urethral calculi admitted to the London Hospital over a twenty year period, from 1910 to 1930, thirty-seven of which were impacted or secondary calculi and only 3 were primary urethral calculi. Thirty-four of 37 cases of secondary calculi were in males and only 3 in females. The 3 primary cases were all associated with urethral stricture of long standing.

Seymour[37] reports the case of a male, aged seventy-one, with a diverticulum of the urethra the size of a hen's egg filled with many stones.

* Presented at the Joint Meeting of the American Roentgen Ray Society and the Radiological Society of North America, Chicago, Ill., Sept. 24–29, 1944.

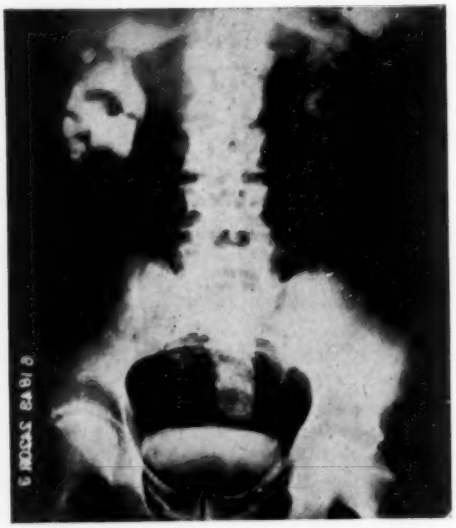

FIG. 1. Case 1. Intravenous urogram showing a large fragmented dendritic calculus completely filling the structures of the right kidney; no excretion from this kidney. The left kidney functions normally.

Heckel and Johannesen[20] report the case of a male, aged sixty-three, with a primary urethral calculus the size of an olive.

d'Offay[11] published the case of a male, aged sixty-six, who nineteen years before, had injured his perineum. He suffered considerable pain following the injury but sought no treatment. Three years later he developed difficulty in passing his water. The stream became very thin one year before admission. He felt a lump in the perineum. The removed stone measured $\frac{7}{8}$ by $2\frac{1}{4}$ inches.

Thomson[10] reports the case of a male, aged fifty-five, who for ten years had passed gravel, with some pain and frequency. The removed urethral stone measured $2\frac{1}{2}$ by $1\frac{1}{2}$ inches. The majority of urethral calculi are associated with local dilatation or diverticulum secondary to chronic obstruction. The generally accepted predisposing cause for all urinary calculi are obstruction, stasis and infection. Many of the reported cases do not specify whether ureteral or urethral stones are primary or secondary. The great majority of these calculi are, however, secondary. We have seen several calculi develop in the site from which a stone had been previously removed undoubtedly due to trauma and associated stasis and obstruction.

CASE REPORTS*

CASE 1. A male, aged sixty-three, was admitted to the Misericordia Hospital, June 17, 1943, because of gastric distress, loss of appetite, general weakness, dyspnea and edema of the ankles. In 1927 the patient had a stone removed from the right kidney. At present, sisteen years after the kidney operation, there is a hard mass easily palpated through the thin relaxed scar in the right kidney region which is especially prominent during coughing or straining, indicating a large incisional hernia. Nearly the entire kidney can be distinctly felt through the herniated relaxed scar. The presence of a large calculus in this kidney was suggested by the surgeon even before the roentgen examination was made. The general condition of the patient was obviously poor. There were no complaints of the patient in regard to the right kidney except that he mentions a lump and big scar in the right kidney area.

Urinalysis: Sp. gr. 1.021, albumin 3 plus, loaded with pus cells, and calcium oxalate crystals.

Roentgen examination of the abdomen shows definite enlargement of the liver. The left kidney is moderately enlarged and unusually dense. The right kidney is apparently normal in size but contains a hugh calculus completely filling the pelvis, calices and uppermost portion of the ureter, all of which structures are greatly enlarged. There is a complete fracture through the base of the upper part of the calculus at its junction with the pelvic portion.

FIG. 2. Case 1. Close-up roentgenogram of the large fragmented dendritic calculus.

* We are indebted to Dr. A. E. Bothe, Genito-urinary Surgeon to the Misericordia Hospital, for permission to report 3 of these cases.

The greatest vertical diameter of this dendritic calculus as measured from the roentgenogram is 12.5 cm.; its greatest transverse diameter 6.5 cm. Intravenous urography shows the appearance of the dye in the pelvis and calices of the left kidney five minutes after the injection. There is no dilatation, obstruction or any other abnormality in the left urinary tract. The bladder is well distended and is normal in contour except for pressure effect on its inferior margin suggesting enlarged prostate. The cortex of the right kidney seems to be reduced to a thin membrane only about 5 mm. in thickness. Six days after admission, a right nephrectomy was performed.

Pathological Report: The entire removed specimen weighed 240 gm. The specimen is completely filled with palpable stones. The calculi from the specimen weighed 100 gm. In the mid-pelvis there is a point of articulation with facetted surfaces. The calices are greatly dilated and contain granular debris. Microscopic section showed marked reduction in stroma and tubular elements. Diagnosis: Nephrolithiasis, pyonephritis. Patient died twenty-four hours after operation of cardiac failure.

Case II. A female aged sixty-three, was admitted to the Misericordia Hospital, August 18, 1940, apparently in good health. About four weeks previous to admission, she sustained a slight back injury in Florida. The roentgen examination at that time showed no evidence of fracture or other injury but she was told that she had a large stone in the right kidney and to see her doctor when she returned to Philadelphia. In 1905 at the age of twenty-eight, patient was pronounced "tubercular" and spent two years in a sanatorium. At the present time patient has only slight backache and is worried about the large right kidney stone. Blood and urine examinations were essentially negative.

Fig. 3. Case II. Plain roentgenogram of the abdomen showing a large heart-shaped opacity in the upper pole of the right kidney.

Fig. 4. Case II. A close-up of the large calcified area which proved to be a healed tuberculous lesion, producing no symptoms.

Roentgen examination, on August 18, 1940, the day of admission shows on the plain abdominal roentgenogram a sharply defined calcified mass 6 by 5 cm. somewhat heart shaped, located either in or on the upper pole of the right kidney. This corresponds in shape and position with the suprarenal gland. Intravenous urography shows the appearance of the dye in the pelvis and calices of both kidneys five minutes after the injection. These structures are reasonably well filled and show nothing abnormal. The thirty-five minute urogram shows good drainage from both sides, no obstruction or any other abnormality. Oblique views show that the calcified body retains the same relation with the upper pole of the right kidney in all views. The possibility of an enlarged calcified adrenal gland is suggested. There were no clinical symptoms to support this possible diagnosis.

August 22, 1940, through a posterior incision,

FIG. 5. Case III. Plain roentgenogram of the abdomen showing the large calculus in the lower portion of the left ureter which developed several years following left nephrectomy. A calculus is also shown in the region from which the left kidney has been removed.

the right kidney was exposed; slightly less than the upper fourth of the right kidney was removed with possible incorporation of the right suprarenal gland. Patient made an uneventful recovery.

Clinical Diagnosis: Tuberculosis of the kidney. Gross description: Specimen consists of a cystic mass measuring 6 by 5 by 3.5 cm. The wall of the cyst is thick and fibrous; the lumen contains a large amount of white pasty opaque fluid. Microscopic examination: The gross findings and histopathologic pictures are consistent with a diagnosis of healed tuberculosis of the kidney. Patient made an uneventful recovery.

CASE III. Female, aged seventy-two, admitted to the Hospital August 22, 1944, because of nausea and vomiting; frequency of urination and burning pain in the bladder region. Temperature, pulse and respiration, normal. Urinalysis: sp. gr. 1.017, negative for albumin, pus cells and casts.

November 14, 1935, patient had a cystostomy for the removal of a vesical stone. April 15, 1936, had left nephrectomy for left renal stone. Patient was again admitted on April 26, 1938, for left retroperitoneal abscess which was incised and drained. The wound continued to drain for many months. November, 1938, the sinus tract was injected with viscid skiodan. This showed a narrow sinus tract communicating with the area from which the kidney had been removed. The kidney bed is represented by an accumulation of the opaque material producing a shadow comparable in size and shape to a gall bladder. The entire left ureter is well outlined with the solution and is moderately dilated down to a point corresponding to the position of the left ureteral orifice. Not any of the skiodan entered the bladder. The sinus tract is therefore communicating with a patent left ureter which is dilated and apparently obstructed at the ureteral orifice. There is a calcified body in the left kidney region. The plain roentgenogram showed an additional laminated calculus about 0.5 cm. in diameter located about 2 inches above the left ureteral orifice.

The recent roentgen examination, August 23, 1944, shows on the plain roentgenogram two calcified bodies, one 1.25 cm., the other 0.5 cm. in diameter located in the left kidney area. There is a large calcified body located in the lower portion of the left ureter 7 cm. in length and slightly more than 1 cm. in its greatest transverse diameter, indicating a large left ureteral calculus.

This calculus has therefore developed from a

FIG. 6. Case III. Intravenous urogram showing good right kidney function as indicated by the amount of dye in the bladder, after about thirty minutes. The large calculus is again shown in the lower portion of the left ureter.

small stone which was present in 1938. At that time the calculus in the lower ureter measured about 0.5 cm. in its greatest diameter. This calculus has developed to its present size since the removal of the left kidney.

Case IV. Male, aged thirty-seven, admitted June 7, 1936, because of pain and swelling in the lower abdomen and general weakness. For the past two years patient has had a sharp pain at frequent intervals in the left side lasting about one hour, gradually becoming more severe and more frequent. For the past two weeks, pain has been constant. Patient has chills, frequency and burning after urination. Past history: General health, fair. Has had four operations for recurring double inguinal hernia. At the age of eight, he fell astride a fire-plug injuring his penis and urethra. Has had sounds passed for urethral stricture since that time up to twelve years ago. On admission, temperature varies from 99 to 102° F.; pulse 80 to 120; respirations 24.

Roentgen examination at this time, twenty-nine years after injury, shows an indistinct outline of the right kidney which appears to be larger than normal. The left kidney outline is not clearly shown, but there seems to be a soft tissue mass in the left kidney area. There is a large calcified body 20 cm. long and 3.75 cm.

Fig. 7. Case IV. Intravenous urogram showing two of the dilated upper calices of the right kidney; no excretion from the left kidney up to one and one-half hours, and a huge articulating calculus in the lower left ureter.

Fig. 8. Case IV. A close-up of the calculus which is probably the largest recorded ureteral stone.

at its widest point, measured from the roentgenogram, located in the lower left quadrant divided by what appears to be an articulation below its middle, apparently located in the lower half of the left ureter. There is also an oval laminated shadow in the region of the lower pole of the right kidney, probably a right renal calculus. Intravenous urography shows the appearance of the dye in the calices of the right kidney ten minutes after the injection. The calices are markedly dilated. Here again the calculus is shown in the lower pole of the right kidney. None of the urograms show any of the dye in the structures on the left side up to one and one-half hours after the injection.

June 7, 1936, under ether anesthesia, a left inguinal incision was made. A large quantity of thick yellow pus was found in the region of the ureter and left kidney area. A rubber tube was inserted for drainage. No attempt was made at this time to remove the large ureteral stone.

July 6, 1936, a suprapubic incision was made to the left of the midline. The bladder was identified and the peritoneum reflected upward by dissection. The left ureter was isolated, incised and opened. The lower of the two calculi was removed, with some difficulty, in one piece. The upper stone was finally removed with great difficulty; this crumbled and was removed by stone forceps and syringe. The removal of the uppermost portion of the stone was followed by the flow of about 350 cc. of yellow thick pus down the left ureter. A large rubber tube was

FIG. 9. Case v. Large calculus in the prostatic portion of the urethra proved by operation.

inserted into the left ureter and connected to a drainage bottle. The prevesical space was packed with gauze and a cigarette drain.

The urine on admission showed from 1 to 2 plus albumin, sp. gr. 1.010 to 1.018, from few to many pus cells, amorphous and triple phosphates; red blood cells 4,500,000; leukocytes from 11,000 to 15,000. Blood chemistry: blood urea nitrogen, 22; blood sugar, 115.

August 12, 1936, nephrectomy was performed through a posterior incision. Pathological diagnosis: Chronic pyonephrosis, left kidney measuring 11 by 6 by 5 cm. Pelvis greatly dilated, calices obliterated.

Drainage was free for the following months and the patient pursued a slow but gradually retrogressive course and died on May 31, 1937.

CASE v. Male, aged twenty-nine, admitted to the Misericordia Hospital, November 7, 1927, with pain in the region of both kidneys of seven months' duration radiating to the scrotum, particularly on the right side. The pain was associated with frequency and burning. He has never noted any blood in the urine and denies venereal infection. He has had night sweats, cough and occasional hemoptysis. Urinalysis: sp. gr. 1.025, heavy trace of albumin, many leukocytes. No tubercle bacilli in sputum or urine. Wassermann test, negative. Temperature, pulse and respiration normal.

Roentgen examination of the chest showed irregular mottled infiltration in the apex of the right upper lobe with contraction of the thoracic cage in this area and lesser involvement in the left apex. The appearance indicates bilateral chronic fibroid tuberculosis.

Roentgen examination of the abdomen and pelvis made November 10, 1927, shows a bullet-shaped calcified body located in the region of the neck of the bladder measuring 3.75 cm. in its longitudinal and 2 cm. in its transverse diameter, indicating a large calculus located probably in the vesical neck. A clinical diagnosis of posterior urethral calculus had been made by the urologist but the location of the concretion on the roentgenogram seemed to be somewhat above the usual position of the prostatic urethra.

Cystoscopic report, November 11, 1927: A grating sensation was felt as a large cystoscope was passed through the posterior urethra. No residue of urine. The bladder neck, mucous membrane and ureteral orifices appeared normal. Trigone is slightly congested. When the scope was withdrawn about one inch from the posterior urethra, a lobulated stone lodged in a diverticulum was seen. Rectal examination revealed the prostate stony hard and nodular. Diagnosis: Large calculus located in a diverticulum in the prostatic urethra.

November 18, 1927, under sacral anesthesia, the calculus was removed through a perineal incision. The prostate was identified, an open-

FIG. 10. Case VI. Two calculi in a diverticulum in the anterior urethra. There are also numerous small calculi in the prostate gland.

ing made into the posterior urethra and the calculus extracted. Patient discharged cured December 19, 1927.

Case VI. Male, aged seventy, admitted to the Misericordia Hospital November 23, 1942, suffering from acute retention of urine. At the age of thirty-six (thirty-four years ago) the patient fell astride a wagon-wheel, rupturing his urethra which was repaired a few days later. No history of venereal disease. At intervals of a few months during the past thirty-four years patient has suffered from attacks of acute retention. At such times a warm bath would enable him to pass a catheter and thus obtain relief. Many sounds have been passed for dilatation of the urethral stricture with no apparent permanent benefit. Temperature, pulse and respiration normal. Urinalysis: sp. gr. 1.015, albumin plus 2; blood urea nitrogen 11.

Intravenous urography November 24, 1942, showed the appearance of the dye in the pelvis and calices of both kidneys five minutes after the injection. There was considerable output after only twenty minutes, indicating good renal function. The bladder wall is slightly thickened and suggests chronic cystitis.

A small roentgenogram made of the bladder area twenty minutes after the injection shows two sharply defined oval calcified bodies, one 1.5 cm., the other 0.5 cm., located in the midline approximately in the middle third of the anterior urethra. There are also a few small calcified bodies beneath the pubic arch suggesting prostatic calculi.

November 25, 1942, patient had acute retention; a catheter could not be passed and a suprapubic cystostomy was performed. A sound was passed through the bladder into the posterior urethra and another sound was passed into the anterior urethra. An incision was made over the sound in the posterior urethra through a dense fibrous stricture and two stones were removed. A suprapubic tube was placed in the bladder and a catheter passed through the penile urethra into the bladder. After four weeks a flexible bougie was passed and the patient was discharged in good condition December 24, 1942.

DISCUSSION

Six cases of unusual urinary tract calculi have been presented. Case I is of special interest because of the large size of the dendritic stone (12.5 by 6.5 cm., weighing 100 gm.); the long period for its development (sixteen years); the marked mobility of the kidney in a large incisional hernia; the recognition of the stone by palpation, and the presence of a fracture which proved to be an articulation.

Case II impressed us as being an odd picture of healed tuberculosis, because of the sharp definition and shape of the dense shadow in the upper pole of the left kidney. There was no disturbance of function or distortion of the pelvis or calices, but there is an old history (thirty-five years ago) of pulmonary tuberculosis. From the roentgen studies calcification of the left adrenal gland was suggested.

Case III is of unusual interest because of the large size of the ureteral concretion (7 by 1.25 cm.); its development for the most part during the six years following left nephrectomy.

Case IV we believe is the largest ureteral stone ever reported. It developed during a twenty-nine year period following an injury to the penis and urethra, several plastic operations and four herniorrhaphies for bilateral recurring inguinal hernias. It developed into two articulating fragments.

Cases V and VI. According to the literature primary calculi in the urethra are rare. In Case V, the large calculus developed in a diverticulum in the prostatic urethra and in Case VI, the two calculi developed in the anterior urethra, posterior to a urethral stricture. With one exception these cases illustrate that obstruction, stasis and infection are the predisposing causes of urinary calculi.

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Vol. 55, No. 2

MASSIVE CALCIFICATION OF THE LIVER*

CASE REPORT WITH A DISCUSSION OF ITS ETIOLOGY ON THE BASIS OF ALVEOLAR HYDATID DISEASE

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A CASE of massive calcification of the liver parenchyma has been encountered recently which is thought worthy of reporting together with a discussion of its probable etiology.

Calcification in many organs of the body is commonly seen on roentgenographic examination, but its occurrence within the liver parenchyma is not. Its occurrence in the liver upon roentgen examination of the abdomen and the etiological factors have been commented upon.[4] In a series of 8,000 autopsies massive calcification of the liver parenchyma was observed only once and its etiology was undetermined.[3]

Echinococcus disease is probably the commonest cause of calcification within the liver and the unilocular variety is by far the most common and most widespread. The unilocular hydatid cyst if unrestricted in its growth is oval or round in shape.[1,2,5] Its wall consists of two layers—an outer chitinous cuticle with characteristic laminations facing the protective fibrous capsule of the host and an inner germinal layer. The growth of the germinal layer by *invagination* produces daughter cysts which contain scolices. These, in turn, may form granddaughter cysts. Around the mother sac of this unilocular cyst a protective fibrous tissue capsule is developed from the tissues of the host. As the parasite grows older and larger, areas of degeneration may occur in the host's capsular tissues. Calcium deposits may be laid down in these areas which may then be observed roentgenographically. They have a curvilinear, round, smooth outline and may form a complete coalescent shell about the parasite. Occasionally some deposition of lime salts may occur in the parasite itself, especially if it has died, but this is generally slight and is not of diagnostic importance compared to the characteristic calcification of the fibrous capsule.

In other organs or tissues of different contrast, such as the lung or bone, the unilocular cyst may be discovered as a rounded area of increased density or as a destructive lesion. In the absence of calcification the diagnosis of echinococcus disease may be made by finding cysts from the ruptured contents. If the cyst can be reached by needle, scolices may be found in the aspirated fluid. While the hydatid is alive it produces antigens which will cause positive skin and complement-fixation tests. When death occurs the antigenic properties may be lost so that the immunologic tests may become negative. If calcification has occurred a positive diagnosis can be made from the characteristic roentgen appearance even in the absence of positive immunologic tests.

In contrast to the unilocular variety met with in all parts of the world, another less common but definite type known as the alveolar hydatid,[1,2,5] occurs in certain geographic areas, especially southern Germany, Switzerland, Czecho-Slovakia, the Tyrol and Eastern Russia. In this type the budding germinal epithelium *evaginates* to form daughter cysts. These are more solid than the daughter cysts of the unilocular variety and contain a jelly-like substance instead of fluid. In addition, there is no distinct fibrous tissue capsule formed by the host like that which encloses the unilocular hydatid. The growth in the organs of the host is infiltrating similar to a malignant neoplasm. Buds may become seeded throughout the liver or carried to some other organ by way of blood or lymph channels. The original area of seeding may develop into a very large mass. With growth the center becomes poorly

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nourished and necrotic, and calcification may then occur. If all of the alveolar hydatid eventually dies, the whole mass may then become calcified and present itself as a large coalescent mass of irregularly calcified bodies of somewhat uniform size. The metastatic hydatids which are usually smaller may also undergo a similar type of calcification upon their death.

Because characteristic calcification of alveolar hydatids has not been generally described, the following case is reported. Although a positive diagnosis could not be established because the skin and complement-fixation tests were negative, it is felt that the type and distribution of the calcification in the liver is best explained by alveolar hydatid disease. The lack of positive immunologic tests can be explained by the complete death of the organism, with loss of antigenic properties. At any rate, the unusualness of the calcification as manifested is enough to warrant its report with the hope that it may stimulate others to report similar findings.

CASE REPORT

The patient is a white soldier, aged thirty-two. He was admitted on March 15, 1944, after having been returned from overseas. There were no specific complaints on admission. However, in February, 1942, he had been admitted to a civilian hospital because of a painless jaundice noted ten days before admission and was in the hospital for thirteen days. He was treated medically. The jaundice gradually cleared and he felt perfectly well after approximately two months. For a year before this illness, he had been in the habit of taking about ten shots of whiskey with beer as a chaser for two or three days on each week-end. At this time he ate very little food. During his treatment in the hospital a routine serological test for syphilis was positive and remained positive after the jaundice cleared. Antiluetic treatment was therefore instituted. The record from the civilian hsopital revealed calcification of the liver on roentgen examination. The patient denies any knowledge of its existence. He gave no history of a primary lesion and denied any knowledge of any illness during his lifetime up to the time of his attack of jaundice. He was born and had lived in Czecho-Slovakia until the age of nine years when he came to the United States.

On induction into the Army the serologic test for syphilis was still positive in spite of the fact that he had had some treatment. A routine course of antisyphilitic therapy was administered following his induction in the spring of 1943. During the course of his treatment he went overseas. Upon the completion of the course in December, 1943, he was admitted to an overseas General Hospital for a final check-up. The spinal fluid was found to be negative but the blood continued to be positive. A physical examination at this time revealed a hard, round mass in the epigastrium which was identified as being connected with the liver. The spleen was also found to be enlarged. Roentgen studies showed that there was a large, irregular, calcified mass in the left lobe of the liver with several smaller calcified masses scattered throughout the right lobe. Gastrointestinal studies were negative with the exception of displacement of the stomach and duodenum by the enlarged left and right lobes of the liver. Laboratory examinations at that time indicated some impairment of liver function.

Because of this enlargement of the liver and the unusual roentgenographic findings, the patient was returned to the United States for further studies.

Here, no additional facts in the history were ascertained. The physical examinations revealed no additional findings. There were no specific complaints and his general state seemed to be fairly good. The various laboratory procedures to estimate his liver function showed that the serum proteins were slightly decreased, the albumin ranging between 3.5 and 4.0 mg. per 100 cc. The cephalin flocculation test was 1 plus in forty-eight hours and another at a later date showed no flocculation. The icteric index was within normal limits. Two hippuric acid tests showed that slightly less than 1 gram of benzoic acid was excreted. All of the blood counts showed normal values for red cells and hemoglobin, but the white cell count showed a persistent leukopenia of moderate degree. The neutrophiles were slightly depressed. The blood serology was again positive. The complement-fixation test for echinococcus was negative. Echinoccoccus antigen for skin testing was not available at this time.

Peritoneoscopy confirmed the presence of the

stony hard mass. The liver surface in addition was somewhat irregular. No biopsy was obtained because of the hardness of the mass.

Roentgenological Findings. The plain abdominal roentgenograms (Fig. 1 and 2) show a rounded 12.0 cm. mottled and irregularly calcified mass in the central portion of the upper abdomen just below the diaphragm which corresponds to the left lobe of the liver. There was no distinct calcified rim or capsule. Scattered throughout the right lobe, but somewhat more posteriorly, are similar areas of calcification. These are not arranged in any discrete mass but are irregularly distributed in the right lobe lying just anterior to the twelfth dorsal vertebra on the lateral projection and range from 1.0 to 2.0 cm. in diameter. No other calcification is noted in any other part of the abdomen. The spleen is also enlarged and extends almost to the iliac crest. The kidney shadows and psoas shadows are normal. Roentgenoscopically, no limitation of the motion of the diaphragm leaf was noted on either side.

Gastrointestinal studies showed no evidence of varix formation of the esophagus. As shown

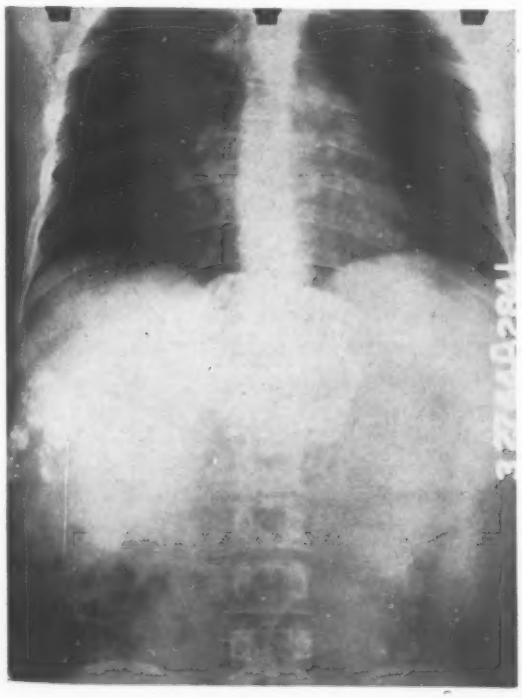

FIG. 1. An anteroposterior abdominal view showing the large coalescent, mottled, calcified mass in the left lobe and the similar smaller more discrete satellite masses in the right lobe. The enlarged spleen is also clearly outlined.

FIG. 2. A lateral view showing the relationship of the calcified masses to the abdominal structures.

in Figures 3 and 4, the body of the stomach presented a normal contour and emptied itself readily. The antrum, pylorus, duodenal cap and proximal duodenum are displaced somewhat anteriorly by the enlarged right lobe of the liver. The distal portion of the descending duodenum and transverse duodenum are in normal position and show no displacement. No intrinsic deformity of the duodenal cap was seen. The large bowel showed no displacement.

These studies did not differ from those previously done overseas. One additional finding was suggested by the present study, and that was the presence in some of the roentgenograms of a round, circumscribed mass of tissue in the medial portion of the right liver lobe, which suggested that the liver may have contained some nodular masses of liver tissue surrounded by a connective tissue capsule.

In October, 1944, the patient was re-studied clinically and roentgenographically. No findings other than those previously described were noted. At this time a skin test with echinococcus antigen, which was obtained from the National Institute of Health, was negative. The complement-fixation test for echinococcus was repeated again and was negative. The liver function tests were again repeated. The total pro-

FIG. 3. Posteroanterior view showing relationship of stomach and upper small intestine to the calcified densities within the liver.

teins were 6.5 mg. per 100 cc. The bromsulfalein excretion was normal.

Infra-red photographs of the abdominal wall showed prominence of the veins supporting the evidence in favor of cirrhosis.

The patient was discharged from the hospital with a diagnosis of cirrhosis of the liver and returned to duty. It was felt that the toxins from the original lesion responsible for the calcified masses in the liver had resulted in injury to liver tissue and that in addition to the calcification of the parasite there was a nodular cirrhosis which had resulted from the liver cell damage.

COMMENT

Since calcification in liver parenchyma is so rare it was difficult to entertain a large differential diagnosis. Several possibilities were considered. Because of the positive serology a luetic cause was considered but calcification does not occur in luetic cirrhosis. Calcified hemangioma was a possibility but there was no bruit. The lack of any history of previous illness seemed to be against an abscess with subsequent calcification of the cavity. Calcification following amebic abscess is not mentioned in the textbooks of pathology. In view of the lack of any history of previous illness and the prevalence of alveolar hydatid disease in the area where this patient lived as a child until the age of nine, it is felt that the calcification in this case is best explained etiologically on this basis. The reason for the lack of supporting immunologic data is discussed above.

FIG. 4. Lateral view showing same relationships. Note the anterior displacement and extrinsic deformity of the proximal duodenum.

CONCLUSION

A case of unusual calcification in the liver is reported, together with a discussion of its etiology on the basis of alveolar hydatid disease.

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Vol. 55, No. 2

CONGENITAL ABSENCE OF PEDICLE FROM THE CERVICAL VERTEBRA

REPORT OF THREE CASES

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VARIOUS types of congenital anomalies are a common finding in the cervical region. These range from the block fusion of two or more adjacent vertebral bodies to the Klippel-Feil syndrome characterized by fusion of numerous segments, hemivertebrae, spina bifida, scoliosis and other deformities. These disturbances of segmentation probably arise in the blastemal or chondral periods of development within the first eight weeks of fetal life.

Another congenital condition, atlanto-occipital fusion, with or without platybasia, may be the cause of neurological symptoms from constriction of the foramen magnum. Foramen distortion may result also from cervical vertebra, a case of which I have previously reported.[1]

Absence of the pedicle is not rare but may remain unrecognized or be misinterpreted and thus cause confusion, especially following an accident. For that reason, the following 3 cases are reported. Case I was briefly described in a previous communication.[2]

The sine quo non is a good pair of stereoscopic 45° oblique studies made with the patient either prone or upright.

REPORT OF CASES

CASE I. A physician, aged thirty-five, forced off the road by a sleepy truck driver, was thrown from his car when it struck a tree. Pain in the neck was only slight, and there was no muscle spasm. There was some limitation of motion, however, upon extreme rotation of the head toward the left. The patient's mother stated that to her knowledge he had never sustained any previous injury. Roentgenograms were at first believed to show a dislocation or a compression fracture although the patient's clinical appearance did not confirm it.

Further roentgen studies of the cervical region, however, were reported as follows: The right side appears normal except for a small fifth foramen and increased density of the fifth arch. On the left side, there is a complete absence of the fifth pedicle with a large foramen at this level. The fourth pedicle is more slender than normal. The cortex of the fifth arch is more dense than the fourth or sixth and lies posterior to their plane. The left sixth superior articular process is somewhat enlarged, and its articulation with the fifth is posterior and above normal position. From this point, the fifth superior articular process extends upward to about $\frac{1}{8}$ inch from the posterior surface of a large, dense fourth inferior articular process rather than articulating with its anterior surface in the normal manner. The customary articular plane slanting from above downward and backward is absent between the fourth and fifth. The fifth transverse process arising from the body in front is well developed but seems to be unattached posteriorly. There is a hyperplasia of the upper left lateral margin of the fifth vertebral body articulating with the fourth body above for greater stability. The flexion extension studies show no localized limitation of movement. There was some list of the cervical spine toward the left side.

CASE II. Female, aged seventy-seven; no history of accident but she complains of pain in the cervical region. Oblique study shows a complete absence of the fifth pedicle on the right side with a long foramen extending from the fourth to the sixth pedicle. A rudimentary transverse process extends backward from the lower margin of the fifth vertebral body toward the fifth and sixth posterior articulation. This divides the large foramen into a middle and a smaller lower portion. A spur from the degenerated fourth disc projects backward into the upper part of the foramen. This upper portion is further encroached upon by the fifth superior articular process which has subluxated forward into it. The entire fifth neural arch is intact. The slender left side of it is to be seen crossing the middle portion of the foramen behind the fifth body. This must not be mistaken for the pedicle.

This patient has advanced intervertebral

disc degeneration with thinning and spur formation of the disc margins. Bony bridging is particularly heavy between the fourth and fifth bodies, doubtless for additional stability. Flexion extension studies show almost complete fixation between all cervical segments below the first and second articulation. There is only a very slight list toward the right side, and rotation is limited.

Case III. This patient, male, aged forty-one, believes condition of neck resulted from a football injury in early life. Pain has become troublesome since straining left shoulder and neck six months ago. The head is held to the left side, and all subjective symptoms are on the left. Besides pain, there is limitation of motion and numbness of the thumb and first finger. The left trapezius muscle is spastic. Rotation and flexion of the neck to the right are painless but limited to less than one-half normal. These movements are somewhat more free toward the left side but produce pain referred down the arm.

Roentgen studies show absence of the third right pedicle. The large foramen extends from the second to the fourth pedicle, but on the roentgenogram it is partially obscured by the rudimentary transverse process arising from the third vertebral body. The right half of the third neural arch is absent, and the left half terminates in a small spinous process. There is some rotation of the second segment with its spinous process displaced toward the right.

Along with the absent pedicle, there are on the right side no articular processes for the third segment. There is, however, a large articular process extending from the second cervical body downward and a somewhat similar mas-

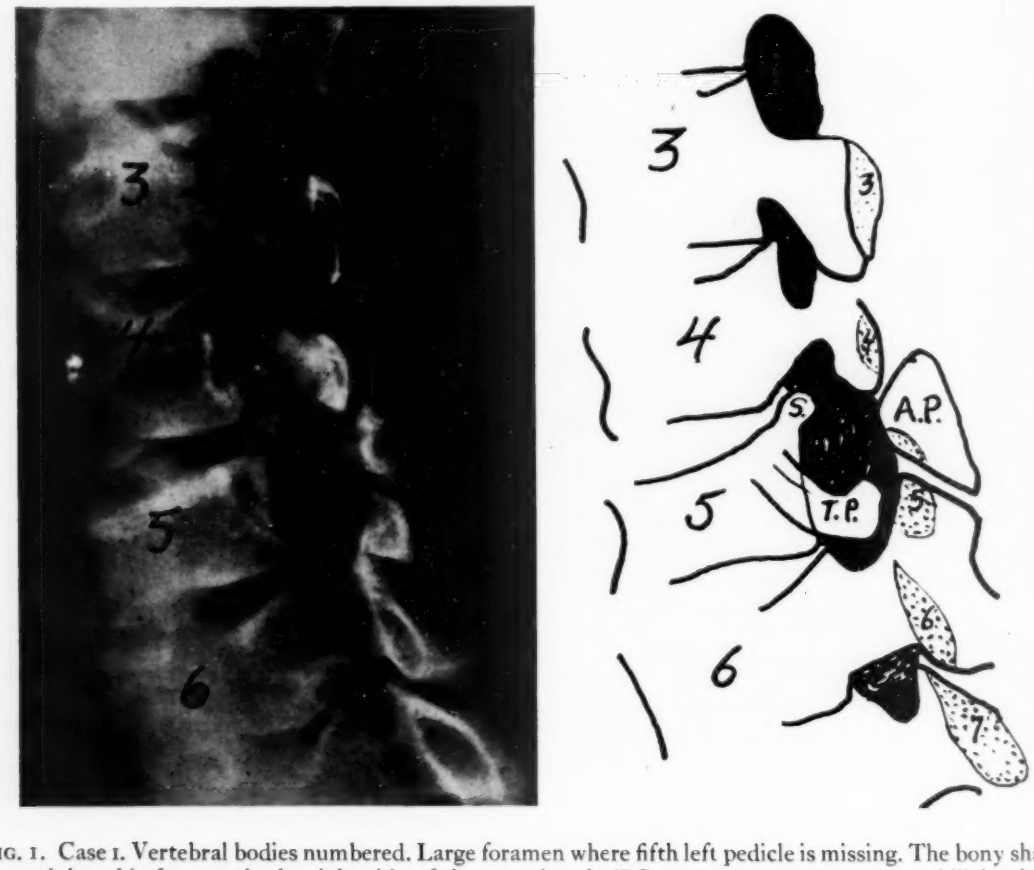

Fig. 1. Case I. Vertebral bodies numbered. Large foramen where fifth left pedicle is missing. The bony shadow overlying this foramen is the right side of the neural arch. *T.P.*, transverse process; *S.*, stabilizing hyperplastic spur articulating with fourth body above. Profiles of the left sides of the neural arches are stippled. *A.P.* is the fifth upper and lower articular processes partly overlying the fifth neural arch.

sive articular process extending from the fourth body upward to articulate with it. These bypass the third body completely. The plane of each one an enlarged intervertebral foramen was visualized on the 45° oblique roentgenogram.

Fig. 2. Case II. Large foramen extending from fourth to sixth pedicle. Fifth right pedicle missing. *N.A.* is the slender left side of the fifth neural arch. This is not the pedicle. *T.P.* indicates the rudimentary transverse process. Encroachment of second foramen by spur from posterior articulation. Encroachment of sixth foramen by spur from degenerated disc. The fifth neural arch (stippled) is displaced forward and upward from its normal alignment with the other arches thereby constricting the upper part of the large foramen. Compare this with the diagram of Case I (Fig. 1) where the involved arch is displaced backward from its normal alignment with the other arches resulting in a foramen much larger in its anteroposterior diameter.

this second-fourth articulation is horizontal. It lies well anterior to the normal posterior articulations, so that when the neck is dorsally extended, its articular surfaces become widely separated but resume contact again upon anterior flexion. There is a distinct list of the spine toward the left side but relatively good movement between the cervical segments.

DISCUSSION

From a study of these 3 cases of absent cervical pedicle, it will be noted that in

The transverse processes were deficient posteriorly. Except in Case II with advanced arthritic changes, movement was relatively free but with some limitation of rotation toward the affected side. The condition per se does not seem to be painful; symptoms in Case II were probably arthritic, and Case III was complaining of pain on the opposite side following injury six months before. The fifth left and the fifth and third right pedicles were missing respectively.

It is interesting to observe how compensation for the resultant weakness was effected. In Case I, the neural arch became more dense and a hypertrophic bone process extended from the margin of the involved vertebral body to that above. Case II developed a heavy bony bridging between the deficient vertebra and the one above, while in Case III, a strong bony column extended from the vertebra above to the one below, completely bypassing the weaker vertebra.

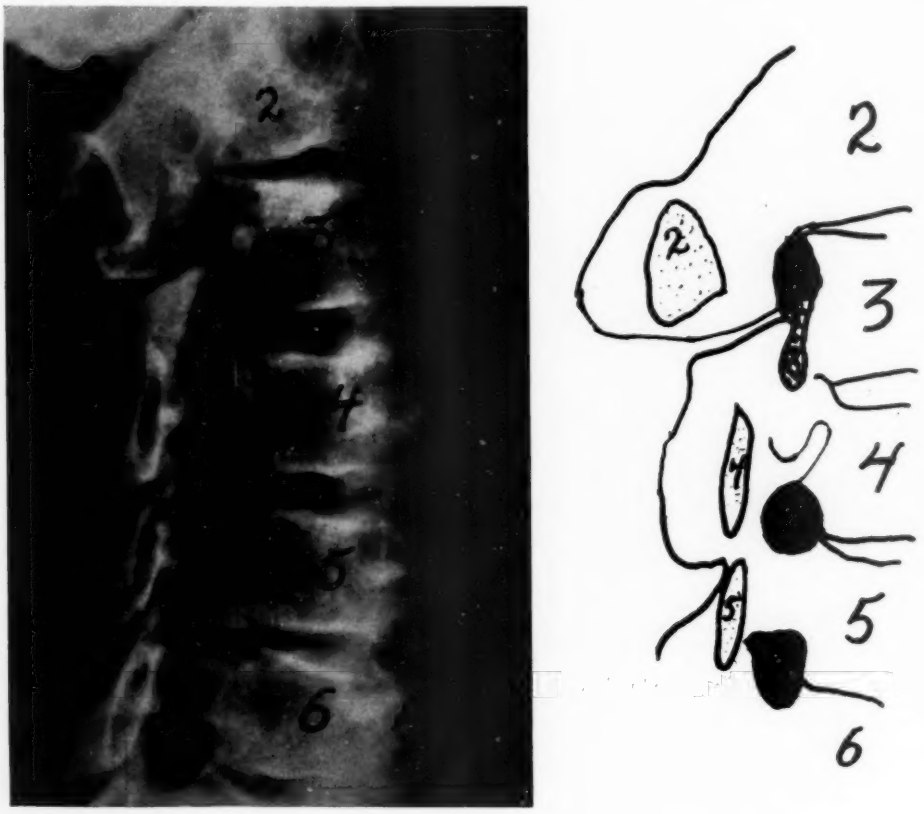

FIG. 3. Case III. Third right pedicle missing. Foramen extending from second to fourth pedicles partly overlaid by third transverse process. Large horizontal articulation between massive second and fourth articular processes. Third neural arch missing, right side (see stippled areas).

In both Cases I and II, the complete neural arches were present and likewise the posterior articulations on the involved side, although one of them was distorted. In Case III, half the neural arch and the articular processes of the weakened side were absent along with the pedicle. In this light, let us consider the matter of early development.

Embryologically,[3] the vertebral segments each develop from three paired centers. These first appear in the blastemal or membranous stage but become well elaborated during the chondral stage before the end of the second fetal month. There are six centers of chondrification, two for the vertebral body, two costal centers for the ribs and one for each side of the neural arch. From each neural arch center, outgrowths develop to form the pedicle, the superior and inferior articular processes, the transverse process and the lamina with its spine.

Ossification begins about the third fetal month. There is usually one center (rarely, two) for the vertebral body and one for

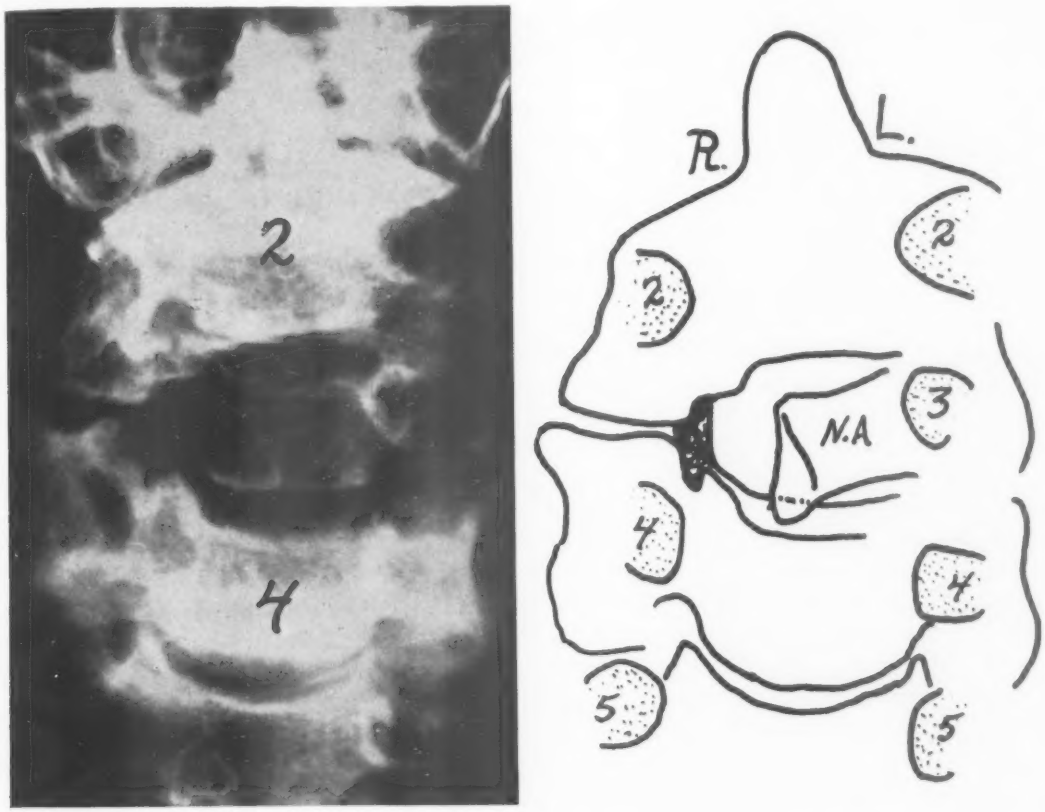

Fig. 4. Case III. Massive second-fourth articulation on right side. *N.A.*, left side of neural arch. Profile of pedicles stippled. Patient has no third pedicle, articular processes or neural arch on right side.

each side of the neural arch. The ribs ossify separately, but in the cervical region, the early chondral rib element remains attached to the vertebral body and joins the early transverse process element to enclose the vertebral artery. This forms the adult type of cervical transverse process.

In the light of this brief statement, it is interesting to evaluate the deficiencies observed in the 3 cases here reported.

In Case III, there was a complete absence of all elements arising from the cartilaginous neural arch center. In Cases I and II, while the pedicle was absent, the lamina and the articular processes had developed, although one of these was deficient in Case I. The transverse processes seemed deficient posteriorly and doubtless originated only from the costal element attached to the vertebral body.

SUMMARY

Congenital absence of the pedicle in the cervical region may be visualized by the 45 degree oblique roentgenogram. There is a resultant enlargement of the intervertebral foramen at this level. This opening may be partially obscured by an overlying transverse process, an exostosis or the lamina on the opposite side.

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THE PROTECTION OF PHOTOFLUOROGRAPHIC PERSONNEL*

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THE widespread use of mass roentgenographic methods in the examination of the chest has introduced several new problems in the field of radiation protection. Operating schedules of photofluorographic equipment frequently exceed five hundred exposures per day, a rate considerably greater than that encountered in general roentgenography. Furthermore, Birnkrant and Henshaw[1] have recently shown that the quantity of radiation required for the exposure of a photofluorographic film is approximately eighteen times greater than that needed for the exposure of a conventional 14×17 inch roentgenogram. It is therefore evident that the radiation hazard to which the personnel of a mass roentgenographic installation are subjected is considerable and that adequate protective measures must be provided to prevent serious radiation injury.

Before protective equipment may be intelligently designed for a roentgen installation, the radiation intensity which prevails in the vicinity of the unit during exposure must be known. In addition, absorption data for a variety of protective materials and pertinent to the range of radiation quality which is expected should be available. Birnkrant and Henshaw have measured the quantity of radiation received at several locations about a photofluorographic unit. The small number of measurements that were taken, however, limits considerably the applicability of their data in many design problems. A small amount of data regarding the absorption of various protective materials under photofluorographic conditions is also available but this, too, is useful only under limited conditions. In an effort to obtain more comprehensive information radiation measurements have recently been conducted on a photofluorographic installation in this laboratory. Sufficient data were obtained to permit the plotting of isodose curves from which the radiation intensity at any location within a large field surrounding the unit may be determined. In addition, absorption curves for lead, iron, aluminum and Masonite presdwood were obtained under actual photofluorographic conditions.

The photofluorograph used in the investigation was a standard 35 mm. Westinghouse model, equipped with a grid and located in the center of a large room, 45 feet long, 35 feet wide and 12 feet high. Floor and walls were of concrete and plaster construction with no wooden structures from which spurious scattered radiation could emanate when impinged upon by the direct roentgen-ray beam; the ceiling was of sheet steel.

The study was initiated by measuring the quantity of radiation received at a number of widely scattered locations within the enclosure when a subject whose chest measured 24 cm. in thickness was photofluorographed with the roentgen machine operating at 100 kv. (peak), 200 ma. and with an exposure time of 0.15 second; measurements were made with a Victoreen ionization chamber having an air capacity of 100 cc. The procedure was then repeated using tempered presdwood phantoms of gradually increasing thickness until the quantities of radiation measured at the several locations were equal to those occurring when the 24 cm. subject was placed in the beam. The phantom which produced an equivalent effect to that of the subject was one 12.5 cm. in thickness and having a surface normal to the roentgen beam, 40

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by 40 cm.* Thereafter throughout the investigation such a phantom was used instead of the human examinee as a scattering agent.

The quantity of radiation to which one is exposed within a photofluorographic room under normal operating conditions was determined by measuring the roentgen intensity at 18 inch intervals throughout the test enclosure when the roentgen tube was operated at 100 kv. (peak) and 25 ma. Ionization measurements were made with a 100 cc. chamber whose ionization current was amplified by a highly stable and highly sensitive vacuum tube circuit.[2] Such an arrangement was sufficiently sensitive to permit the accumulation of readings with but one exposure per location and with the roentgen tube operating under conditions which allowed the rapid recording of data from the large number of locations studied without excessive heating of the tube. The readings taken in this way of course indicate only the roentgen intensity received under the special conditions of the test and require conversion to roentgens per normal photofluorographic exposure before they become useful. Such conversion was obtained by multiplying the data by a factor derived in the following manner: The quantity of radiation received at a particular location was measured by conventional procedure when an exposure was made in which the roentgen tube operated at 100 kv. (peak) and 30 mas. (the exposure previously found to produce a photofluorogram of optimum density of the 24 cm. subject). A reading was then made with the chamber-amplifier apparatus at the same location with the roentgen tube operating at 100 kv. (peak) and 25 ma. The ratio of the first reading to the second represents the desired conversion factor.

The ionization chamber with which all of the foregoing data were obtained was constructed of bakelite having a wall thickness of 1.8 mm. The absorption of such a thickness of bakelite when tested with the scattered radiation produced by the phantom was slightly less than 5 per cent. Accordingly, the various results were multiplied by an additional factor of 1.05 to correct the readings to so-called "air-wall" conditions.

The results of the investigation are illustrated graphically in Figure 1 where the quantities of radiation received at various locations about a photofluorograph are charted. The data expressed in roentgens per one hundred exposures are plotted as isodose curves. These data apply not only in the horizontal plane as shown but in any plane located radially about the longitudinal axis through the photofluorograph. Thus the radiation conditions occurring in rooms above and below the unit may be derived merely by locating on the chart the position of the rooms relative to the photofluorograph and reading the dosage rate at that point. For example, the quantity of radiation to which an individual is subjected when located in a room 9 feet directly above the roentgen tube is slightly less than 0.014 r per one hundred exposures.

The contours of the several isodose curves are of considerable interest. Directly behind the roentgen tube the dosage rate is relatively low, and rises to rather high levels as one progresses laterally. Also at a position directly lateral to the photofluorographic screen there is a sharp change of curve configuration with a progressive diminution of the dosage rate as one advances to the left parallel to the photofluorographic camera. These phenomena point unmistakably to the conclusion that the radiation to which operating personnel are exposed within the photofluorographic enclosure is scattered radiation originating within the subject under examination. Behind the roentgen tube this radiation is of relatively low intensity because of the shielding which the tube affords. Similarly, the dosage rate in the region of the photofluorographic camera is extremely low

* The equivalence of the radiation measurements made with this phantom on the one hand and the subject on the other was surprisingly close at the several locations not only when the tests were made at a single kilovoltage but when the procedure was repeated at 80 and at 90 kv. (peak), and with and without the use of a beam-limiting cone.

because of the very considerable shielding which the large photofluorographic hood provides. The sharp change in the contour of the curves which occurs lateral to the hood may also be ascribed partly to the shielding of the hood and also to the shielding of the subject's lateral tissues which fall outside the direct beam and therefore have a small shielding effect. Where there is no shielding, i.e. along a line extending posteriorly and laterally from the subject, the dosage rates are relatively high.

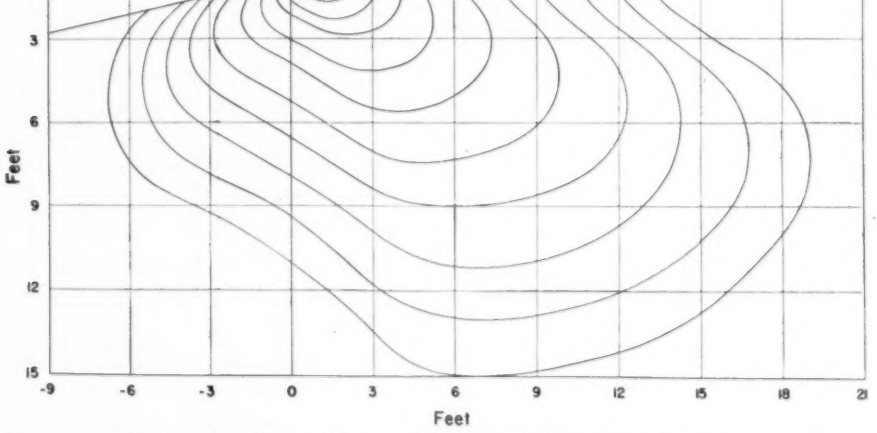

FIG. 1. Isodose curves illustrating the exposure conditions which exist about a photofluorographic installation. Data indicate the quantity of radiation, in roentgens, received per one hundred exposures at various locations about the unit.

The data illustrated in Figure 1 apply strictly only to a 35 mm. photofluorograph, roentgenographing patients 24 cm. in thickness, with the roentgen tube operating at 100 kv. (peak), with a cone limiting the roentgen beam, with a grid incorporated in the photofluorographic hood and with scattering material within the enclosure reduced to a minimum. Under other operating conditions the data will be modified in the following manner:

(*a*) Other types of photofluorographic equipment: The quantity of radiation required for the exposure of 70 mm. and 4 by 5 inch photofluorograms is from 25 to 50 per cent greater than that needed for the exposure of 35 mm. film. Accordingly, the dosage rates are correspondingly greater than those shown in Figure 1 for such equipment.

(*b*) Other types of patients: A subject 24 cm. in thickness was deliberately chosen for this study because such an individual is somewhat larger than average and accordingly the data so obtained will tend to present values somewhat greater than those normally encountered. A desirable factor of safety will thereby be introduced.

(*c*) Other roentgen tube voltages: When measurements were made with roentgen tube potentials of 90 kv. (peak) and 80 kv. (peak), dosage rates respectively 20 per cent and 40 per cent higher than those obtained at 100 kv. (peak) were obtained. These observations may seem somewhat paradoxical because it is well known that scattered radiation originating within a medium diminishes as the roentgen tube potential decreases. Actually, measurements of roentgen intensity indicated just such a diminution but the exposure times required for the production of photofluoro-

grams of optimum quality were prolonged to such an extent when the kilovoltage was lowered that the quantities of radiation increased by the amounts listed above.

(*d*) Conditions when a cone, limiting the roentgen beam, is absent: Birnkrant and Henshaw[1] have reported an increase in the dosage rates of from 27 to 48 per cent when a limiting cone is not used. Measurements made during this investigation confirmed these observations and revealed an average increase of 30 per cent.

(*e*) Conditions when a grid is not incorporated in the photofluorograph: The absence of a grid decreases the average photofluorographic exposure by approximately 50 per cent with a corresponding diminution in the dosage rates. Since conventional practice demands the use of a grid routinely in order to improve film quality, this fact is hardly of sufficient significance to bear notation.

(*f*) Conditions when the walls of the photofluorographic enclosure receive the direct roentgen beam: When the direct roentgen beam falls on the walls of the photofluorographic room, the dosage rates will be increased. This effect will be particularly marked when the walls are of wooden or cellulose construction. Dosage rates, 50 to 100 per cent higher than those shown in Figure 1, were observed opposite the photofluorographic hood and camera in the peripheral portions of the enclosure when a wooden wall, ½ inch in thickness, was placed behind and to the side of the camera. This effect of course may be easily eliminated by restricting the roentgen beam with a lead-impregnated flange of relatively small dimensions surrounding the photofluorographic hood immediately behind the plane of the screen.

Although the information provided by Figure 1 is of considerable interest it does not permit the design of protective screens for use in photofluorographic installations without absorption data on available protective materials. As a part of the current investigation, absorption curves were obtained on lead, steel, aluminum and Masonite presdwood. These curves were derived from measurements made with the ionization chamber-amplifier circuit used in obtaining the dosage rate data and with radiation scattered from the 12.5 cm. presdwood phantom when irradiated with a roentgen tube operating at 100 kv. (peak). This radiation therefore was identical in quality to that encountered in actual photofluorographic practice. In these studies, the ionization chamber was enclosed in a lead container, in one side of which was a portal, 10 by 15 cm., which restricted the entrance of radiation to that emanated by the phantom.

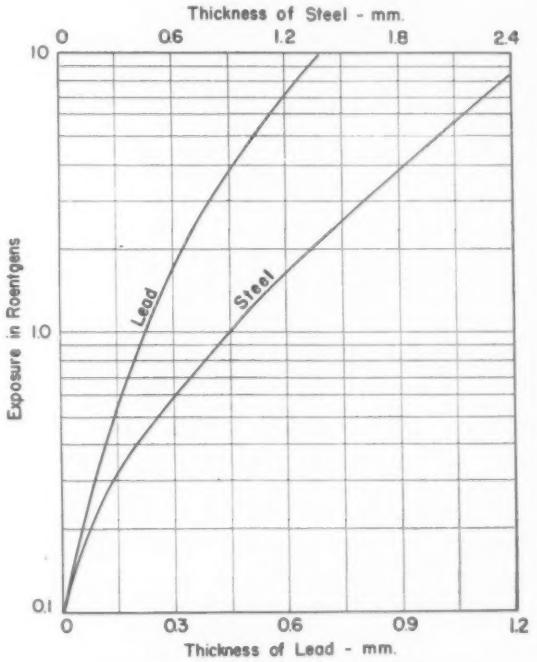

FIG. 2. Thicknesses of lead and steel required to reduce various quantities of radiation received about a photofluorographic installation to 0.1 r.

The absorption data for lead and steel are plotted in Figure 2, where the thickness of lead and steel required to reduce the quantity of radiation received at any location to 0.1 r is plotted against the dosage received at that location. For example, if the quantity of radiation received at a particular position is 1.0 r, it will be reduced to 0.1 r by 0.22 mm. of lead or 0.9 mm. of steel.

The maximum daily dose of roentgen radiation which may be tolerated by an individual operating roentgen equipment has been arbitrarily established at a level of 0.1 r per day.[3] From Figures 1 and 2, then, the minimum requirements for the construction of photofluorographic protective screens may be easily calculated for any location in which operating personnel may wish to work. For example, an unprotected person working immediately behind the roentgen tube of a photofluorograph which has an average operational rate of five hundred exposures per day would receive 0.40 r per day (i.e., 0.08×5 r per day). Reference to Figure 2 indicates that the protective screen at this location should include lead at least 0.1 mm. in thickness, or steel 0.4 mm. in thickness.

The relatively small thicknesses of lead and steel which are required for adequate protection has prompted some people to consider aluminum as a protective material. Absorption measurements, however, indicate that a thickness of aluminum approximately ninety times that of lead is required for equivalent absorption. The use of aluminum is therefore not feasible economically nor from the standpoint of weight.

Absorption measurements of Masonite presdwood (density = 1.07) indicate that the absorption of this material is less than 0.1 per cent of that of lead. It is therefore apparent that persons working in rooms separated only by wooden or cellulose walls, floors or ceilings from a photofluorographic installation require serious consideration when the problems of protection are considered. When the separating partitions are of concrete (density = 2.4) or brick the absorption of these materials will be approximately 1.0 per cent and 0.5 per cent respectively of lead.[4] It is unlikely then that when these building materials are used any added protective measures will be required, unless the wall is impinged upon by the direct roentgen-ray beam, since the thickness of partitions made with these materials usually exceeds 2 to 4 inches.

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VOL. 55, NO. 2

THE CALCULATION OF DOSE FROM POINT AND LINEAR SOURCES OF RADIUM*

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METHODS for the calculation of dose from point and linear sources of radium have been published by several physicists. These methods all possess a high degree of accuracy but are somewhat complex in their practical application. It is therefore of advantage to group together the pertinent data and to simplify the physical formulas to a point consistent with the accuracy permitted by our present knowledge of the subject and our limited technical facilities.

The calculation of dose in gamma-ray therapy depends upon the fundamental rule that the intensity of gamma radiation from a point source of radium varies inversely as the square of the distance from the source and directly as its strength. The dose at any given point is equal to the product of the intensity at that point and the time of application.

$$I \alpha \frac{M}{h^2}$$

$$D = I \times t$$

where I = intensity at point $\mathcal{Q}$ (Fig. 1),
M = strength of radium source, usually measured in milligrams,
h = distance of $\mathcal{Q}$ from M, usually measured in centimeters,
D = dose at point $\mathcal{Q}$,
t = time of application, usually measured in hours.

The gamma roentgen, r_γ, is now generally accepted as the unit of dosage in radium therapy. The relation between the gamma roentgen and the strength of a radium source is given in the rule that the intensity of gamma radiation 1 centimeter from a 1 milligram point source of radium filtered by 0.5 millimeter of platinum is 8.4 gamma roentgens per hour. This value may be termed the gamma roentgen conversion factor for gamma rays of radium filtered by 0.5 millimeter of platinum. The conversion factors for other filters may be calculated from the absorption formula:

$$C = 9.0 \times e^{-ud}$$

where C = conversion factor,
u = absorption coefficient of gamma rays of radium in filter used,
d = thickness of filter.

The conversion factors for the more commonly employed filters of platinum, calculated from this formula, are given in Table 1. These factors apply only to gamma radiation. The effects of primary and secondary beta radiation are not considered. With a primary filter of 0.5 mm. platinum, or 1.0 mm. lead, or 2.0 mm.

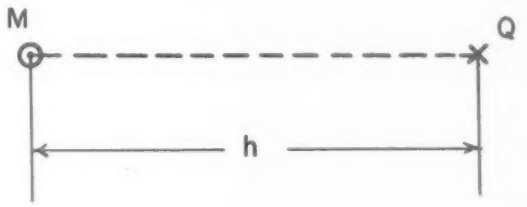

FIG. 1.

TABLE I

CONVERSION FACTORS FOR VARIOUS PLATINUM FILTERS OR EQUIVALENT

Thickness of Platinum Filter	Conversion Factor—C
0.0 mm.	9.0
0.3 mm.	8.6
0.5 mm.	8.4
0.6 mm.	8.2
0.8 mm.	8.0
1.0 mm.	7.7
1.5 mm.	7.2
2.0 mm.	6.7

* From the Department of Radiotherapy, Mount Sinai Hospital, New York.

TABLE II

PLATINUM-EQUIVALENT FACTORS FOR VARIOUS METALS AND ALLOYS

Metal or Alloy	Platinum-Equivalent Factor
Platinum	1.0
Platinum-iridium	1.0
Gold	1.0
Lead	0.5
Silver	0.45
Nickel	0.25
Copper	0.25
Monel metal	0.25
German silver	0.25
Brass	0.25
Steel	0.22
Tin	0.22
Zinc	0.22
Aluminum	0.1

brass, practically all of the primary beta radiation is absorbed.

The amount of secondary beta radiation originating in the primary filter is at a minimum with elements of intermediate atomic number, such as steel, nickel, copper, zinc or tin. Quimby, Marinelli and Blady have shown that these elements produce less secondary beta radiation than elements of high atomic number, such as lead, gold or platinum, or those of low atomic number, such as hydrogen, carbon, oxygen, and so forth, which are found in rubber, wax, bakelite, and similar substances. The secondary beta radiation is absorbed almost entirely in the first 1 or 2 millimeters of tissue.

If other metal filters are employed instead of or in combination with platinum, the conversion factors can be calculated from the absorption formula. However, an approximation sufficiently accurate for radium therapy may be obtained by an estimation of the thickness of platinum which gives the same amount of absorption of gamma rays as the thickness of metal used. The platinum-equivalent thickness may be determined by multiplying the thickness of the filter by its platinum-equivalent factor, which is given in Table II.

The factor of absorption in tissue and similar substances, such as wax, wood, water and lead-free rubber is complicated by an increase of radiation due to scatter. The exact value in any particular case can be determined only by actual measurement. However, from data published by Failla, Laurence, and Sievert, an approximation sufficiently accurate for radium therapy can be made. This is best expressed in the form of a factor (S) for varying thicknesses of tissue, as given in Table III.

From this data, the "point source formula" may be derived for the dose in gamma roentgens delivered by the gamma radiation from a point source of radium at any given distance.

$$D=\frac{M\times t\times C\times S}{h^2} \qquad (1)$$

where D = dose in gamma roentgens at point $\mathcal{Q}$ (Fig. 1),
M = milligrams of radium,
t = hours of application,
C = conversion factor for filter used,
S = tissue factor (if radiation is in air, this factor = 1.0),
h = distance in centimeters between the radium source and point $\mathcal{Q}$.

TABLE III

TISSUE FACTORS FOR VARIOUS THICKNESSES OF TISSUE

Thickness of Tissue	Tissue Factors—S
1.0 cm.	0.98
2.0 cm.	0.95
3.0 cm.	0.94
4.0 cm.	0.93
5.0 cm.	0.92
7.0 cm.	0.89
10.0 cm.	0.84
15.0 cm.	0.75
20.0 cm.	0.67

Conversely, the number of milligram-hours of radium (or millicurie-hours of radon) required to deliver a specified dose in gamma roentgens at any given distance from the point source may be calculated from the same formula.

If radon is used instead of radium, the equivalent number of millicurie-hours may be calculated from the radon disintegration formula if radon decay tables are not available:

$$M\times t = Mc\times[1-e^{-0.00755t}]\times 133$$

where $M\times t$ = equivalent number of millicurie-hours,
Mc = number of millicuries at beginning of application,
t = time of application, in hours.

For permanent implants, the exponential factor becomes zero.

$$M\times t = Mc\times 133.$$

If the permanent implants are in the form of gold or platinum seeds with a wall thickness of 0.3 mm., a useful modification of the point source formula may be derived for the number of millicuries required to deliver 1,000 r_γ at any given distance.

$$Mc \text{ per } 1000\ r_\gamma = \frac{1000\times h^2}{133\times 8.6} = 0.88\times h^2. \quad (1A)$$

In this formula the factor for tissue absorption is not included since it is slight for the range of activity generally required of seeds.

A formula for the calculation of dose from a linear source of radium, such as a needle or a tandem, may be derived mathematically from the point source inverse square law. In any linear source, the active length must be known. If several sources are used in a line, the over-all active length should be measured. In Figure 2, the active length of this 2.2 cm. capsule is 1.6 cm., whereas, in Figure 3, the over-all active length of a tandem of three such capsules is 6.0 cm.

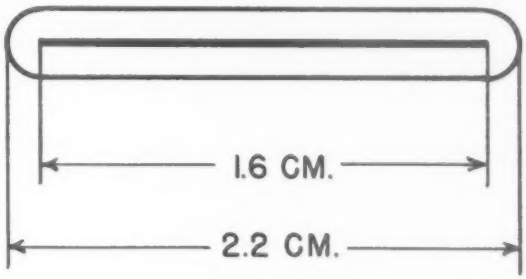

FIG. 2.

For the derivation of the formula, it is essential that the radium be evenly distributed; that is, the linear density, or the number of milligrams of radium per centimeter, should be uniform. Where a linear source is made up of several capsules or needles in a line, as illustrated in Figure 3, the inactive gaps, AB, should be made as small as possible. An inactive gap equal to "0.5 h" (see Fig. 4 for definition of "h") introduces an error of 5 to 10 per cent.

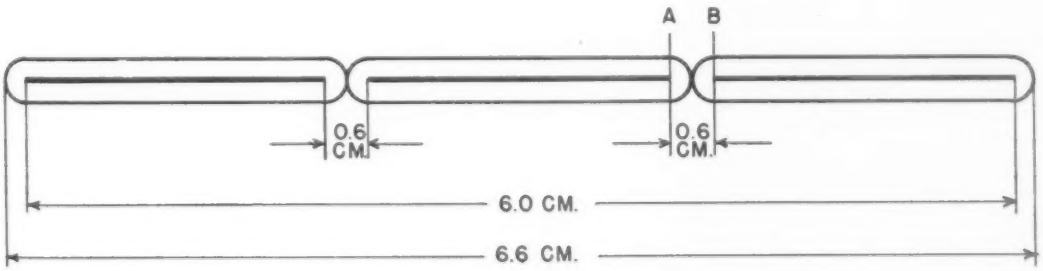

FIG. 3.

The basic method of calculation of the dose from a linear source is the division of the active length into a number of small segments. The contribution to the total

dose from each segment is calculated from the point source formula, each segment being considered as a point source. The dose is then the sum of the contributions from all segments. This is the method employed by Quimby and Mayneord and Honeyburne, but it requires considerable arithmetical labor. If the linear source is not of uniform linear density, it is the only accurate method. However, if the linear density is uniform, Sievert's formula is more accurate and simpler to apply. The following method is an adaptation of the Sievert formula to conditions commonly met with in radium therapy. It has been further modified to give the dose directly in gamma roentgens.

A linear source (Fig. 4) containing M milligrams of radium, uniformly distributed, measures L centimeters in overall-active length. From the point $\mathcal{Q}$, at which the dose is to be determined, a perpendicular is drawn to the line L. This perpendicular measures h centimeters and divides line L into two segments, a and $L-a$. In this manner, the position of point $\mathcal{Q}$ is defined with reference to the linear source. The intensity from a small segment, dx, situated x centimeters from the intersection of h with L is determined from the point source formula. The amount of radium in this segment is $(M/L)dx$, and the intensity, i, is, therefore:

$$i=\frac{M}{L}\times\frac{dx}{r^2}\times C\times S$$

where r = distance from dx to $\mathcal{Q}$.

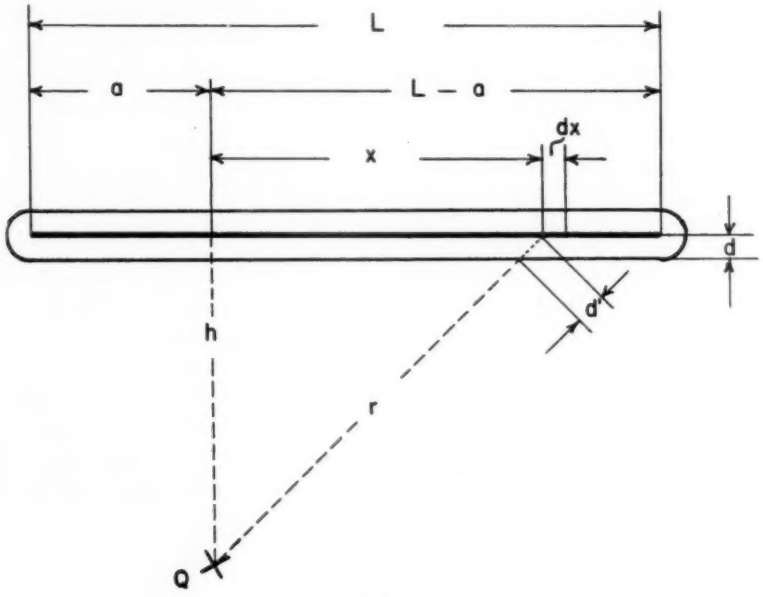

Fig. 4.

Since the gamma rays from dx to point $\mathcal{Q}$ traverse the filter obliquely, for a path d^1 instead of d, the wall thickness of the filter, the conversion factor C must be separately calculated.

$$C=9.0\times e^{-ud^1}.$$

However,

$$d^1=d\times\frac{r}{h}$$

and

$$r^2=h^2+x^2$$

$$\therefore i=\frac{M}{L}\times\frac{dx}{h^2+x^2}\times 9.0\times\left[e^{\frac{-ud\sqrt{h^2+x^2}}{h}}\right]\times S.$$

The total intensity is obtained by integration of this expression. The limits of the integral are those which define line L;

TABLE IV

RATIO FACTORS FOR VARIOUS FILTRATIONS OF PLATINUM OR EQUIVALENT

Ratio	Ratio Factor—f (ratio)				
$\frac{L-a}{h}$ $\frac{a}{h}$		$f\frac{L-a}{h}$	$f\frac{a}{h}$	$f\frac{L}{h}$ or $f\frac{L}{2h}$	
$\frac{L}{h}$ or $\frac{L}{2h}$	No Filter	0.5 mm. Pt	1.0 mm. Pt	1.5 mm. Pt	2.0 mm. Pt
10.0	13.22	11.45	10.00	8.84	7.82
8.0	13.01	11.34	9.95	8.78	7.81
6.0	12.65	11.12	9.82	8.73	7.77
5.0	12.36	10.93	9.69	8.65	7.71
4.5	12.17	10.78	9.60	8.58	7.67
4.0	11.93	10.62	9.48	8.49	7.60
3.5	11.64	10.40	9.31	8.35	7.50
3.0	11.24	10.09	9.06	8.17	7.34
2.5	10.71	9.67	8.72	7.90	7.12
2.0	9.96	9.04	8.21	7.47	6.76
1.8	9.57	8.71	7.93	7.22	6.55
1.6	9.11	8.31	7.58	6.93	6.30
1.5	8.84	8.07	7.37	6.75	6.15
1.4	8.57	7.82	7.15	6.55	5.98
1.3	8.25	7.53	6.90	6.34	5.79
1.2	7.88	7.23	6.63	6.09	5.57
1.1	7.50	6.88	6.32	5.81	5.33
1.0	7.07	6.49	5.98	5.51	5.05
0.9	6.60	6.07	5.59	5.16	4.74
0.8	6.08	5.59	5.16	4.76	4.39
0.7	5.50	5.07	4.68	4.34	3.99
0.6	4.86	4.49	4.15	3.83	3.54
0.5	4.17	3.85	3.56	3.27	3.05
0.4	3.43	3.16	2.93	2.71	2.51
0.3	2.62	2.42	2.25	2.08	1.93
0.2	1.77	1.65	1.53	1.42	1.31
0.1	0.90	0.84	0.77	0.72	0.67

that is, as x varies from $-a$ to $L-a$. The integration was performed graphically by Sievert. The "linear source formula" may therefore be written in the following form:

$$D=\frac{M\times t}{L\times h}\times\left[f\left(\frac{L-a}{h}\right)+f\left(\frac{a}{h}\right)\right]\times S \qquad (2)$$

where D is the dose in gamma roentgens.

The expressions, $f([L-a]/h)$ and $f(a/h)$, represent functions which take into account the effect of oblique filtration and the effect of the varying distance of the point from successive minute segments of the linear source. Since it is a ratio that is involved, i.e. length of the source to distance of the point from the source, the formula holds for any length of source and any distance (except zero). The values of these functions may be calculated from Sievert's data and are given in Table IV for the more commonly employed filtrations of platinum or equivalent and for ratios varying from 10:1 to 1:10. The values for other filtrations of platinum and for ratios intermediate between those given in the table may be obtained by interpolation. These values may be called "ratio factors." The ratio factors have been calculated so that the formula reads directly in gamma roentgens.

Ratios greater than 10:1 are seldom encountered in radium therapy whereas

for ratios less than 1:10, the point source formula is equally as accurate and simpler to use. For a ratio of 1:3, the error involved in using the simpler point source formula is about 5 per cent. Therefore, for practical purposes, a linear source may be considered as a point source if the distance at which the dose is determined is more than three times the length of the source.

The tissue factor, S, to be used in the linear source formula may be obtained from Table III for the distance h. This distance is a suitable average for the at any given point may be calculated from the linear source formula.

The ratio factors may also be used to estimate the relative doses at points along a line parallel to the linear source. The doses in the midplane, i.e. at point Q_1, Figure 5, are always maximum for any given distance h

$$\frac{D \text{ at point } Q_2}{D \text{ at point } Q_1} = \frac{f\left(\frac{L-a}{h}\right)+f\left(\frac{a}{h}\right)}{2f\left(\frac{L}{2h}\right)}.$$

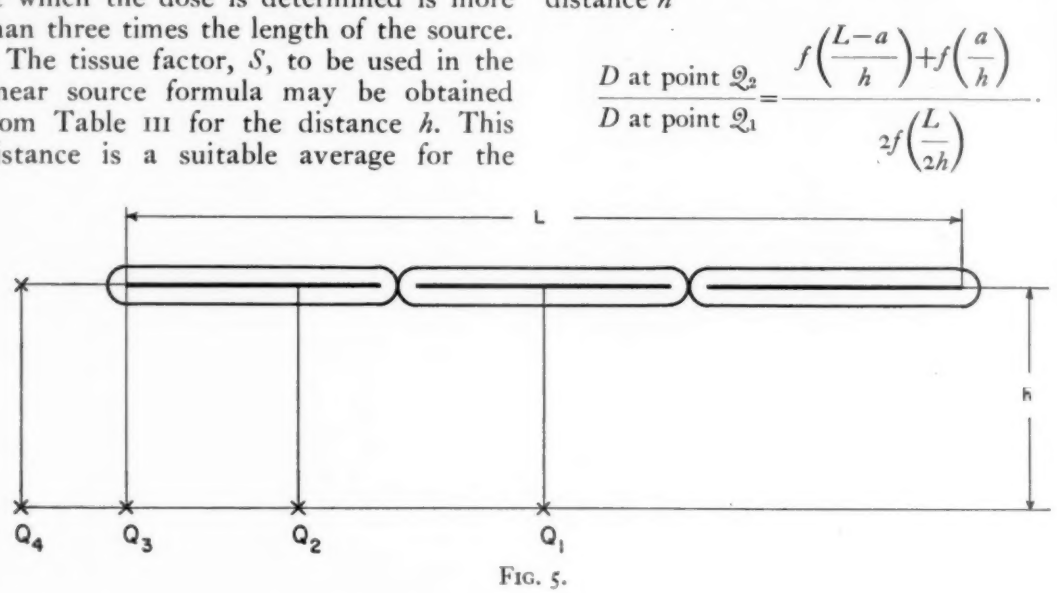

Fig. 5.

effect of tissue absorption, since the tissue factor is, at best, a rough approximation.

For points beyond the end of the linear source, e.g. point Q_4, Figure 5, the segment a is the length of the extension from line L to the perpendicular from the point. Algebraically this segment is negative. Therefore, when its value is substituted in the linear source formula, the proper algebraic sign must be observed (see example 2 D).

For points (Q_1, Fig. 5) in a plane at right angles to the midpoint of the linear source, a equals $L/2$. The ratio factors are therefore simplified to $2f(L/2h)$. Similarly, for points (Q_3, Fig. 5) in a plane at right angles to one end of the linear source, a equals zero, and the ratio factors are therefore simplified to $f(L/h)$.

Conversely, the number of milligram-hours of radium (or millicurie-hours of radon) required for a linear source to deliver a specified dose in gamma roentgens

Discussion

The point and linear source formulas, while mathematically accurate, are based upon certain assumptions and factors which limit their accuracy in practical radium therapy.

The formulas are based upon a theoretical point or line without thickness. An error is therefore introduced because of the dimensions of the radium source. Radon seeds are generally regarded as point sources but they usually measure 3 to 4 mm. in length. A needle or capsule may have an inner diameter varying from 0.5 to 1.5 mm. Since distance measurements are made from the central axis of the source, calculations for points closer than 0.5 cm. are subject to a large error. For distances greater than 0.5 cm., however, the error is small enough to be disregarded. Another source of error lies in the possible uneven distribution of the radium in the needle or capsule. This can sometimes be demon-

strated in an autoradiograph.

The conversion factors depend upon the values of the absorption coefficients, except the factor for 0.5 mm. of platinum which was obtained experimentally. The experimental values for this filtration range between 8.0 and 8.6. The value of 8.4 appears to be the mean and is therefore accepted for this article. There are no "accepted" values of the absorption coefficients. Kohlrausch found the absorption coefficient for platinum to be 2 cm.$^{-1}$, Mayneord and Honeyburne 1.5 cm.$^{-1}$, and Laurence 1.39 cm.$^{-1}$. Laurence states that the value obtained by Kohlrausch cannot apply to radium therapy because the effect of scattered radiation from the filter was not considered. For this article, the value of 1.5 cm.$^{-1}$ was accepted arbitrarily and used in the calculation of the conversion factors in Table I. The differences between these values and those obtained by employing a coefficient of 2 cm.$^{-1}$ or 1.39 cm.$^{-1}$ are given in Table V.

For metals other than platinum, the absorption coefficients obtained by Laurence are quite at variance with those published by Sievert (who quotes Kohlrausch). Quimby obtained the platinum-equivalent thicknesses without determining the values of the absorption coefficients. The experimental set-up employed by Quimby approximates the conditions under which radium is often used in therapy. Therefore the platinum-equivalent factors in Table II were calculated from Quimby's data. These factors are sufficiently accurate for radium therapy provided not more than 2 mm. of filter are used.

The tissue factors cannot be determined accurately by any simple formula. The increase of radiation due to scatter invalidates the use of the tissue absorption coefficients determined by Kohlrausch and Failla. Sievert included the tissue absorption coefficient in his calculation of dose from point and linear sources, but, in so doing, omitted the contribution from scattered radiation. The amount of scattered radiation depends upon the total volume and character of the tissue irradiated. It cannot be calculated by any simple method and must therefore be measured. Such measurements were made by Laurence for various thicknesses of tissue. The tissue factors in Table III were obtained from Laurence's data by averaging the various values given for each thickness of tissue. At best, they must be considered rough approximations.

Finally, the measurement of distances in tissue cannot be made with precision because of practical difficulties. An error of 10 per cent in a distance measurement may mean an error of about 20 per cent in the dose calculation.

TABLE V

DIFFERENCE BETWEEN CONVERSION FACTORS CALCULATED WITH $u = 1.5$ CM.$^{-1}$ AND THOSE CALCULATED WITH OTHER VALUES OF PLATINUM ABSORPTION COEFFICIENT

Thickness of Platinum Filter	Percentage Difference	
	$u = 2.0$ cm.$^{-1}$	$u = 1.39$ cm.$^{-1}$
0.0 mm.	+3%	0
0.5 mm.	0	0
1.0 mm.	−2%	+1%
1.5 mm.	−4%	+1%
2.0 mm.	−7%	+2%

From this discussion, it is obvious that the calculation of dose in radium therapy is limited in accuracy by inherent and practical difficulties which require consideration in the evaluation of the final result.

The following examples illustrate a few of the applications of the point and linear source formulas.

Example 1. If a single capsule of radium, with a primary filter of 1.0 mm. of platinum, a secondary filter of 2.0 mm. of brass, and an active length of 1.6 cm., is placed in a cervical stump for 3,000 mg-hr., the dose delivered to the obturator node, estimated at 5.0 cm. from the cervical canal, may be calculated as follows:

The point source formula may be employed

since the distance is more than three times the active length of the source.
Platinum-equivalent factor for brass = 0.25
Equivalent filtration of 2.0 mm. brass = $2 \times 0.25 = 0.5$ mm. Pt
Total filtration = $1.0 + 0.5 = 1.5$ mm. Pt
Conversion factor for 1.5 mm. Pt = 7.2
Distance = 5 cm.
Tissue factor for 5 cm. = 0.92
Therefore,

$$D = \frac{M \times t \times C \times S}{h^2} = \frac{3000 \times 7.2 \times 0.92}{5^2} = 795 \text{ r}_\gamma.$$

Example 2. A linear source consists of three 15 mg. capsules of radium in a rubber tandem. The primary filter is 1.0 mm. of platinum. The over-all active length measures 6.0 cm. The time of application is 100 hours. The doses at various points in a line 3 cm. from the linear source and parallel to it may be calcualted as follows:

A. At a point in the midplane (point $\mathcal{Q}_1$, Fig. 5)

$M = 45$ $L = 6.0$ S (for 3 cm.) $= 0.94$
$t = 100$ $h = 3.0$

$a = \frac{L}{2} = 3$ $\frac{a}{h} = 1$ $f(1)$ for 1.0 mm. Pt $= 5.98$

$L - a = 3$ $\frac{L-a}{h} = 1$ $f(1)$ for 1.0 mm. Pt $= 5.98$

$$D = \frac{M \times t}{L \times h} \times \left[f\left(\frac{L-a}{h}\right) + f\left(\frac{a}{h}\right) \right] \times S$$

$$= \frac{45 \times 100}{6 \times 3} \times [5.98 + 5.98] \times 0.94$$

$$= 2800 \text{ r}_\gamma$$

(For this problem, the ratio factors are equivalent to $2f(L/2h)$)

B. At a point 1.0 cm. from one end of the linear source (point $\mathcal{Q}_2$, Fig. 5)

$a = 1.0$ $\frac{a}{h} = 0.33$ $f(0.33)$ for 1.0 mm. Pt $= 2.48$

$L - a = 5.0$ $\frac{L-a}{h} = 1.67$ $f(1.67)$ for 1.0 mm. Pt $= 7.70$

$$D = \frac{45 \times 100}{6 \times 3} \times [7.70 + 2.48] \times 0.94$$

$$= 2390 \text{ r}_\gamma$$

C. At a point in the end plane (point $\mathcal{Q}_3$, Fig. 5)

$a = 0$ $\frac{a}{h} = 0$ $f(0) = 0$

$L - a = 6$ $\frac{L-a}{h} = 2$ $f(2)$ for 1.0 mm. Pt $= 8.21$

$$D = \frac{45 \times 100}{6 \times 3} \times 8.21 \times 0.94$$

$$= 1930 \text{ r}_\gamma$$

D. At a point 1.5 cm. beyond the end of the linear source (point $\mathcal{Q}_4$, Fig. 5)

$a = -1.5$ $\frac{a}{h} = -0.5$ $f(-0.5)$ for 1.0 mm. Pt $= -3.56$

$L - a = 7.5$ $\frac{L-a}{h} = 2.5$ $f(2.5)$ for 1.0 mm. Pt $= 8.72$

$$D = \frac{45 \times 100}{6 \times 3} \times [8.72 - 3.56] \times 0.94$$

$$= 1210 \text{ r}_\gamma$$

Example 3. The relative doses at the various points described in Example 2 may be estimated from the ratio factors, the midplane dose being taken as 100 per cent.

D at point $\mathcal{Q}_1 = 100\%$

$$D \text{ at point } \mathcal{Q}_2 = \frac{7.70 + 2.48}{2 \times 5.98} \times 100$$

$$= 85.1\% \text{ of } D \text{ at point } \mathcal{Q}_1$$

$$D \text{ at point } \mathcal{Q}_3 = \frac{8.21}{2 \times 5.98} \times 100$$

$$= 68.6\% \text{ of } D \text{ at point } \mathcal{Q}_1$$

$$D \text{ at point } \mathcal{Q}_4 = \frac{8.72 - 3.56}{2 \times 5.98} \times 100$$

$$= 43.1\% \text{ of } D \text{ at point } \mathcal{Q}_1$$

These percentages check exactly with the actual doses obtained in Example 2.

Example 4. The number of milligram-hours of radium required to deliver 700 gamma roentgens to a point 5.0 cm. from the midpoint of the tandem used in the previous examples may be calculated as follows.

$L=6.0 \qquad h=5.0 \qquad S=0.92$

$a=\frac{L}{2} \quad \therefore \text{ ratio factors}=2f\left(\frac{L}{2h}\right)$

$\frac{L}{2h}=0.6 \quad f(0.6) \text{ for 1.0 mm. Pt}=4.15$

$D=700$

$$700=\frac{M\times t}{6\times 5}\times 2\times 4.15\times 0.92$$

$\therefore M\times t=2750$ mg-hr.

SUMMARY

The following formulas have been derived for the calculation of dose from point and linear sources of radium in terms of the gamma roentgen:

1. The point source formula

$$D=\frac{M\times t\times C\times S}{h^2}$$

2. The linear source formula

$$D=\frac{M\times t}{L\times h}\times\left[f\left(\frac{L-a}{h}\right)+f\left(\frac{a}{h}\right)\right]\times S$$

A few useful simplifications of these formulas have also been derived.

The various factors concerned are given in the form of tables.

The significance of the various factors is discussed.

The limitations of accuracy of the formulas were analyzed.

Several examples were given to illustrate the application of the formulas.

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I wish to express my appreciation to Mr. Carl B. Braestrup and Dr. Sergei Feitelberg, physicists, Mount Sinai Hospital, for their helpful criticism and for their assistance with the mathematics and physics in this article.

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Issued Monthly. Subscription $10.00 per year, $11.00 in Canada and $12.00 in foreign countries. Advertising rates submitted on application: Editorial office, 110 Professional Building, Detroit, Mich., Office of publication, 301–327 East Lawrence Avenue, Springfield, Ill. Information of interest to all readers will be found on page iv.

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Representatives on American Board of Radiology: Douglas Quick, New York, N. Y., B. P. Widmann, Philadelphia, Pa., F. W. O'Brien, Boston, Mass.

Twenty-eighth Annual Meeting: 1946, to be announced.

EDITORIAL

TUMORS AND TUMOR METASTASES IN THEIR RELATION TO TRAUMA

OUR advances in knowledge are a great stimulus to a revision of various subjects in medicine which have previously been accepted as established facts, and in no field of so-called established knowledge has this fact been more evidenced than in a re-assessment of mechanical trauma in its relation to bone tumors or bone metastases. Ewing,[1] several years ago, pointed out that "many recent fundamental contributions on the causation of tumors have an important bearing on the relation of trauma to cancer. When nothing definite was known about the effective exciting factors in mammary cancer it was permissible to adopt the traumatic theory in cases in which the clinical evidence pointed strongly that way." With our recent advancement in the experimental production of mammary cancer, particularly in mice, the traumatic origin becomes much less tenable. It is possible to produce cancer experimentally with many agents but always under specific conditions that are not related to trauma, and the experimental data reveal that the genesis of cancer requires quite peculiar factors which have not been found in the results of trauma, and the accumulation of knowledge thus gained has modified our views concerning cancers and their possible relation to simple traumas.

Quite recently, Saphir, Appel and Levinthal[2] have made an experimental attempt to localize tumor metastases in long bones by mechanical trauma. They state that there are many references containing discussions dealing with the influence of trauma on tumor development, and numerous reports indicating that in some unexplained manner trauma may be a significant factor in initiating malignant growth, but that there are relatively few articles concerning the influence of trauma on the localization of metastases. Their experiments were carried on with this idea in mind. They were stimulated in their experimental researches by the conflicting evidence of relation of trauma to metastases and because of the importance of this problem from the medicolegal standpoint.

Their particular experimental study was undertaken "to ascertain whether or not trauma applied to long bones might be influential in the localization of metastases from a transplanted malignant tumor." In their experiments the Brown-Pearce rabbit tumor was used, for obvious reasons, namely that it is a highly malignant tumor, readily transplanted into the testes, from which it metastasizes early. In their experiment attempts were made to localize the metastases in long bones by a single mechanical trauma and also by chronic irritation. In their experimental animals bone metastases have not been observed in their stock tumor rabbits except in the spinal column, and then but rarely. When, however, they transplanted fragments of the Brown-Pearce carcinoma into the long bones (the femur) directly, the tumor grew well within the marrow spaces in all cases, soon invaded the periosteum and adjacent muscles, and metastasized extensively.

In a number of rabbits the left humerus was fractured and immediately afterwards

[1] Ewing, J. Modern attitude toward traumatic cancer. *Arch. Path.*, 1935, *19*, 690–728.

[2] Saphir, O., Appel, M., and Levinthal, D. H. Attempts to localize tumor metastases in long bones by mechanical trauma. *Cancer Research*, 1945, *5*, 722–723.

[3] Jones, F. S., and Rous, P. On the cause of the localization of secondary tumors at points of injury. *J. Exper. Med.*, 1914, *20*, 404–412.

an intravenous injection of a suspension of tumor cells was made into the ear vein. These rabbits were followed both clinically and roentgenographically. Roentgenograms of the entire skeleton of each rabbit were made after death. In those animals, at autopsy, which had received the intravenous transplantation, most of the metastases were found in the lungs, but the kidneys and liver were also involved. The region of the experimental fracture was carefully examined by means of roentgenograms in the gross, and a number of block sections were taken from the region of the fracture and the adjacent bone and soft tissue. There was no macroscopic evidence of tumor in this location. The histological examination revealed tremendous cellular proliferation in the region of the fracture and callus formation, which varied according to the interval between the time of fracture and the death of the animal. In several cases serial sections were cut from the region of the fracture but in none of these cases was there evidence of tumor cells at the site of the fracture.

To see what part chronic mechanical irritation might possibly play in the localization of tumor metastases, they introduced a piece of a small vitallium screw immediately beneath the periosteum in close contact with the cortex of the distal end of the femur. This screw was held in place by silk sutures and was placed so that with each movement of the leg the metal rubbed against the bone. In all of their experimental animals the position of this screw was verified by roentgenograms. Upon the death of the animals the position of the screw was studied again by means of roentgenograms to be sure that it had remained in place. A thickened periosteum, evidence of mechanical irritation, was almost invariably noted, and again widespread metastases were recorded, but no gross evidence of tumor was encountered in any of the animals at any point of the mechanical irritation. Multiple sections taken from the bone in the area of the mechanical irritation and examined histologically revealed no evidence of tumor cells.

From these experiments the investigators concluded that mechanical trauma or chronic irritation of bones played no rôle in the localization of metastases from transplanted Brown-Pearce carcinomas in rabbits.

While it is not always easy to transfer animal experiments to the human, it is at least significant that the experimental data presented by Saphir and his associates quite closely agree with the ideas of many other observers, particularly Ewing, who has cautioned us that "Opinions regarding the possible traumatic origin of any tumor must be based on a full consideration of the location, known conditions of origin, structural peculiarities and clinical course of the tumor in each organ," that further generalizations may be invalid or misleading, that the interpretation of compensation laws should recognize that trauma is never the sole cause of cancer and is often only a subordinate, although determining cause, that the probability of coincidence is great, that aggravation by injury is rare and difficult to establish, and he emphasizes the fact that there is urgent need of more competent detailed analysis of individual cases of tumors that are possibly traumatic.

The experimental work of Saphir and his associates lends great weight to Ewing's discussion and it is such experimental work coupled with clinical observations that will in all probability lead us to a proper perspective regarding trauma and its relation to cancer or tumor formation.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Sept. 17–20, 1946.

American College of Radiology
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago.

Section on Radiology, American Medical Association
Secretary, Dr. U. V. Portmann, Cleveland Clinic, Cleveland, Ohio. Annual meeting: San Francisco, Calif., July 1–5, 1946.

Arkansas Radiological Society
Secretary, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark. Meets every three months and also at time and place of State Medical Association.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: 1946, to be announced.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

Section on Radiology, California Medical Association
Secretary, Dr. Gordon G. King, 3700 California St., San Francisco 18, Calif.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

Radiological Section, Los Angeles County Medical Association
Secretary, Dr. Roy W. Johnson, 1407 S. Hope St., Los Angeles, Calif. Meets on second Wednesday of each month at the County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N.Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

Chicago Roentgen Society
Secretary, Dr. F. H. Squire, 1754 W. Congress St., Chicago 12, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. Carroll C. Dundon, 2065 Adelbert Road, Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

Dallas-Fort Worth Roentgen Study Club
Secretary, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meetings held in Dallas on odd months and in Fort Worth on even months, on third Monday, at 7:30 P.M.

Denver Radiological Club
Secretary, Dr. A. Page Jackson, Jr., 1612 Tremont Place, Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

Florida Radiological Society
Secretary, Dr. J. F. Pitman, Blanch Hotel Annex, Lake City, Fla. Meetings in May and November.

Georgia Radiological Society
Secretary, Dr. James J. Clark, 478 Peachtree St., Atlanta, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meets annually second Sunday in May.

Iowa X-Ray Club
Secretary, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Michigan Association of Roentgenologists
Secretary, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. Annette T. Stenstrom, 1218 Medical Arts Bldg., Minneapolis, Minn. One meeting a year at time of Minnesota State Medical Association.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

New Hampshire Roentgen Ray Society
Secretary, Dr. Richard C. Batt, Berlin, N. H. Four meetings a year.

Radiological Society of New Jersey
Secretary, Dr. H. R. Brindle, 501 Grand Ave., Asbury Pk. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

New York Roentgen Society
Secretary, Dr. Ramsay Spillman, 115 East 61st St., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. An-

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

nual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

North Dakota Radiological Society
Secretary, Dr. L. A. Nash, St. John's Hospital, Fargo. Meetings held by announcement.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

Ohio Radiological Society
Secretary, Dr. Henry Snow, 1061 Reibold Bldg., Dayton, Ohio. Meets during annual meeting of Ohio State Medical Association.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport.

Philadelphia Roentgen Ray Society
Secretary, Dr. C. L. Stewart, Jefferson Hospital, Meetings first Thursday of each month, October to May, at at 8:00 P.M., in Thomson Hall, College of Physicians, 21 S. 22d St.

Pittsburgh Roentgen Society
Secretary, Dr. L. M. J. Freedman, 4800 Friendship Ave. Meets 6:30 P.M. at The Ruskin on second Wednesday, each month, October to May inclusive.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Murray P. George, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary Dr. A.M. Popma, 220 N. First St., Boise, Idaho.

St. Louis Society of Radiologists
Secretary, Dr. Edwin C. Ernst, Beaumont Medical Building, St. Louis, Mo. Meets fourth Wednesday of each month, except June, July, August, and September, at a place designated by the president.

San Diego Roentgen Society
Secretary, Dr. Henry L. Jaffe, Naval Hospital, Balboa Park, San Diego, Calif. Meets monthly on first Wednesday at dinner.

San Francisco Radiological Society
Secretary, Dr. Carlton L. Ould, University of California Hospital, San Francisco 22. Meets monthly on the third Thursday at 7:45 P.M., first six months of the year at Lane Hall, Stanford University Hospital, and second six months at Toland Hall, University of California Hospital.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting, Dallas, Texas, Monday, January 14, 1946.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. E. L. Flanagan, 116 E. Franklin St., Richmond, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Thomas Carlile, 1115 Terry St., Seattle. Meets fourth Monday each month, October through May, College Club, Seattle.

X-ray Study Club of San Francisco
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly, third Thursday evening.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Medical Members' meeting held monthly on third Friday at 2:30 P.M. and Ordinary Meeting at same time on following Saturday, October to May, 32 Welbeck St., London, W.1.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month at 4:45 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

Canadian Association of Radiologists
Secretary, Dr. J. W. McKay, 1620 Cedar Ave., Montreal, P. Q.

Société Canadienne-Francaise d'Electrologie et de Radiologie Mídicales
Secretary, Dr. Origène Dufresne, 4120 Ontario St., East Montreal, P. Q.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Sociedad Peruana de Radiologia
Secretary, Dr. Victor Giannoni, Apartado, 2306, Lima, Peru. Meetings held monthly except during January, February and March, at the Asociación Médica Peruana "Daniel A. Carrión, Villalta, 218, Lima.

Continental Europe

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. Babaiantz, Geneva.
Secretary for German language, Dr. Max Hopf, Effingerstrasse 49, Bern. Meets annually in different cities.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad: USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

SECOND INTER-AMERICAN CONGRESS OF RADIOLOGY

A letter just received from Dr. Pedro L. Fariñas, President of the Second Inter-American Congress of Radiology to be held in Havana, Cuba, November 17–22, 1946, states that he would like to have as soon as possible the names of the authors and titles of the papers which will be contributed from the United States. There is room for a limited number of papers on the program and it is suggested that all members of the American Roentgen Ray Society who expect to attend this Congress next November and who wish to present a paper, communicate *at once* with the undersigned, so that titles of papers may be sent to the central committee at Havana. Because of the long distances involved and the time consumed for transmission of the mails, it is necessary to issue the printed program much earlier than would ordinarily be the case, and a tentative program must be printed in the very near future.

It is therefore requested that all who plan to attend the Congress and give a paper or all who plan to make a contribution to the scientific exhibit, communicate with the undersigned at the earliest possible date.

James T. Case, M.D., Chairman
General Committee for the United States
20 North Wacker Drive
Chicago 6, Illinois

SECOND INTER-AMERICAN CONGRESS OF RADIOLOGY

November 17–22, 1946

Hotel Nacional, Habana, Cuba

PROGRAM OF THE SCIENTIFIC MEETINGS AND SOCIAL EVENTS

Sunday—November 17, 1946

From 2 to 6 P.M. Registration at the Headquarters of the Congress at the National Hotel, first floor.

GENERAL ASSEMBLY

9:00 P.M. Silver Room. The Honorable Dr. Ramón Grau San Martín, President of the Republic of Cuba, will deliver the opening address.

9:30 P.M. The President of the past "First Congress of Radiology," Dr. José F. Merlo Gómez, from Argentina, will proceed to turn over the Presidency to the President-elect of the "Second Inter-American Congress of Radiology," Dr. Pedro L. Fariñas, from Havana.

10:00 P.M. Presentation to the Audience of the Official Delegates.

11:00 P.M. Address "Radiology in America," by Dr. James T. Case.

12:00 M. Buffet.

Monday—November 18, 1946

9:00 A.M. Presentation of papers. There will be *six* papers. The maximum time alloted for each presentation is 20 minutes.

12:00 M. Reception at City Hall by the Mayor of Havana. Group lunches will be given by Officers of the Congress.

9:00 P.M. Official Symposium on the Diagnosis of *Cancer of the stomach*. The opening paper of the symposium will be allotted 30 minutes. There will be three more papers on the same subject with 20 minutes for each one of them.

Tuesday—November 19, 1946

9:00 A.M. Presentation of papers. There will be *six* different papers. The maximum time allotted for each presentation is 20 minutes.

1:00 P.M. Lunch and typical Cuban Fiesta at one of the beach clubs.

4:00 P.M. Official symposium on the Diagnosis and Treatment of *Bone Tumors*.
The opening papers of the symposium will be allotted 30 minutes.
There will be three more papers on the same subject with 20 minutes' time for each one of them.

9:00 P.M. *Lecture*—Solemn session at the Hotel's Silver Room celebrating the

fiftieth anniversary of the discovery of X-Rays by Roentgen. The lecture will be delivered by the delegate of the Republic of Colombia.

WEDNESDAY—NOVEMBER 20, 1946

9:00 A.M. Presentation of papers. There will be *six* different papers. The maximum time allotted to each one of them is 20 minutes.

12:00 M. Lunch at the Country Club.

4:00 P.M. Official Symposium on Diagnosis and Treatment of *Bronchogenic carcinoma*.

The opening paper of the symposium will be allotted 30 minutes.

There will be three more papers on the same subject with 20 minutes' time for each one of them.

9:30 P.M. Concert by the Philharmonic Orchestra of Havana. Eric Kleiber conducting.

THURSDAY—NOVEMBER 21, 1946

9:00 A.M. Presentation of papers. There will be *six* different papers. The maximum time allotted for each presentation is 20 minutes.

1:00 P.M. Group lunches given by Officers of the Congress.

4:00 P.M. Official Symposium *Radiological mass survey*.

The opening paper of the symposium will be allotted 30 minutes.

There will be three more papers on the same subject with 20 minutes time for each one of them.

9:00 P.M. The Annual Banquet with entertainment and dancing at the National Casino.

FRIDAY—NOVEMBER 22, 1946

9:00 A.M. Presentation of papers. There will be six different papers. The maximum time allotted for each presentation is 20 minutes.

12:00 M. Visit to a Sugar Mill and typical country life entertainment, cock-fights, etc. Lunch in the country.

9:00 P.M. Council meeting for the Foundation of the *Inter-American College of Radiology*.

Executive and Business sessions.

Elections.

SATURDAY—NOVEMBER 23, 1946

Free morning to visit the city and its surroundings.

3:00 P.M. Visit to Oriental Park. Race Track where Radiological handicap will be run.

Tea at the Jockey Club.

NOTES ON THE PROGRAM

The scientific program of the Second Inter-American Congress of Radiology will be closed the 31st July, 1946. Please be kind enough to send, before that date, the title of your paper with an abstract of the paper not exceeding one hundred words, which abstract will be published in the final program.

The program of the Scientific Exhibit will be closed on the 31st July. Send the title or your Exhibit and also a detailed description of the material. The x-ray films must be presented in reductions of 5×7 inches. Each film should carry its own description.

The Commercial Exhibit will display the best on modern equipment and x-ray accessories. We have rented space for the leading x-ray concerns.

Transportation facilities have been asked from and promised by Pan American Airways. You, as a Congressman, are entitled to a discount of 15% on your ticket over the usual 10% discount for round trip fare. Please write our Secretary as soon as possible confirming your decision to come, so we will be able to make reservations at the hotel.

The Congress fee is $10.00 (U. S. dollars). You can either send the money directly to us or through your x-ray society, or also pay at our Registration Booth in Havana.

Members notifying their participation will be met at the airport by members and ladies of the Reception Committee. We will assist you in any formalities with the Immigration authorities and will take care of your arrival at the National Hotel.

It has been decided that all meetings and official social gatherings will be absolutely informal. Due to difficulties in transportation light luggage is suggested.

The climate in November in Cuba is so mild that nearly every day you can enjoy beach recreation. There is no need for an overcoat, bring your spring clothes, they are all right for our climate in winter. The ladies may bring light furs.

Besides the scientific and social events officially stipulated in the program, we have also organized several entertainment and cultural gatherings for

all to enjoy. All exclusive Clubs and Casinos will be open to Congressmen and their families.

Officials and ladies of the Social Committee will have the great pleasure of assisting anybody interested in visiting the historic monuments, churches, museums, clubs, beaches, government buildings, etc., or may have the intention of buying anything in our Department Stores.

Ladies will have their Registration desk next to the Registration Booth of the Congress on the first floor of the National Hotel.

Our traditional Cuban hospitality will not fail. You may be sure that your Havana winter days will be unforgetable.

CANCER TEACHING DAY

A Cancer Teaching Day will be held at the Hotel Jamestown, Jamestown, New York on Thursday, February 28, 1946. This is presented under the auspices of the Medical Society of the County of Chautauqua, Jamestown Medical Society, Medical Society of the State of New York, and the New York State Department of Health, Division of Cancer Control. The meeting will be called to order at 2:30 P.M., and the paper of the afternoon will be presented by Louis C. Kress, M.D., Director, State Institute for the Study of Malignant Diseases, Buffalo, New York, on "What the Public Should Know about Cancer."

Dinner will be served at the Hotel Jamestown at 6:30 P.M. Advance reservations are required.

The evening meeting will begin at 8 P.M. at which the following two papers will be presented: "Malignancies of the Uterus" by Clyde L. Randall, M.D., Professor of Gynecology, University of Buffalo School of Medicine, Buffalo, New York; "Cancer of the Breast" by Samuel J. Stabins, M.D., Assistant Professor of Surgery, University of Rochester School of Medicine and Dentistry, Rochester, New York.

MESSAGE FROM THE SOVIET UNION

The following cable was recently sent by the radiologists of the Soviet Union to American radiologists on the occasion of the fiftieth anniversary of the discovery of the roentgen ray. The message was transmitted by the American Soviet Society to the Secretary of the American Roentgen Ray Society who in turn submitted it for publication in this JOURNAL:

On the occasion of the fiftieth anniversary of the discovery of the x-rays and radioactivities American roentgenology, on marking this momentous date this January, all Soviet roentgenologists and radiologists—numbering many thousands—warmly greet their overseas colleagues in the United States. Soviet biology highly appreciates great contribution made to treasury of world roentgenology and radiology by our American colleagues during the past half century. Soviet roentgenologists and radiologists have always closely followed notable achievements and progress of their American coworkers in this field. We sincerely wish our American friends every success in their further work.

PROFESSOR S. REINBERG
On Behalf Jubilee Committee

UROLOGY AWARD

The American Urological Association offers an annual award "not to exceed $500" for an essay (or essays) on the result of some specific clinical or laboratory research in Urology. The amount of the prize is based on the merits of the work presented, and if the Committee on Scientific Research deem none of the offerings worthy, no award will be made. Competitors shall be limited to residents in urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years. All interested should write the Secretary, for full particulars.

The selected essay (or essays) will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Netherland Plaza, Cincinnati, Ohio, July 22–25, 1946.

Essays must be in the hands of the Secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis 3, Tennessee, on or before July 1, 1946.

Committee on Scientific Research
JUDSON B. GILBERT
ANSON L. CLARK
MILEY B. WESSON, *Chairman*

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

NEURO-OPHTHALMOLOGY. By Donald J. Lyle, B.S., M.D., F.A.C.S., Lecturer on Neuro-Ophthalmology, Department of Anatomy, Medical College of the University of Cincinnati; Attending Ophthalmologist to the Good Samaritan Hospital, Christ Hospital, Jewish Hospital, St. Mary's Hospital and Children's Hospital. Cloth. Price, $10.50. Pp. 398, with 529 illustrations. Springfield, Illinois: Charles C Thomas, 1945.

For years Dr. Lyle's exhibits in neuro-ophthalmology have adorned the scientific exhibit sections of medical conventions. Out of these exhibits, which have grown from year to year in scope and depth, has developed the book on Neuro-Ophthalmology which lies before us. In it the author has endeavored to bring together "in brief, but comprehensive and coordinated matter," the many phases of neurology that make up neuro-ophthalmology. The author's own background in neurology is dominantly an anatomical one which he acquired as a pupil of A. R. Vonderahe, at the University of Cincinnati. It is, therefore, not surprising that neuro-anatomy figures very prominently in Lyle's Neuro-Ophthalmology, with neurophysiology and theories of all kinds keeping well in the background.

Another characteristic of the book is the abundant factual material which is included in the form of 130 case histories and which makes for greater practicality, lucidity and vividness of the text. In 126 of these cases the diagnosis had been confirmed by the findings at operation or autopsy. Extensive use has been made of combined illustrations showing for instance, on the same page, the ophthalmoscopic picture and the perimetric, roentgenologic or autopsy findings. The ophthalmoscopic findings have been recorded in black and white, stereoptic or single photographs of the fundus. Because of the importance of color in ophthalmoscopic diagnosis, it is hoped that in future editions the black and white fundus photographs will be replaced with kodachrome pictures.

Aiming at comprehensiveness, the author has perhaps included more elementary ophthalmology than would have been necessary in a book of this kind. His first chapter, for instance, entitled, "Embryological Development of the Neural Structure of the Eye," while it represents a logical starting point for the book, contains chiefly fundamental ophthalmology. Outstanding chapters, from the standpoint of the ophthalmologist, are the ones dealing with the arterial vascular system of the brain and the presentation of the cerebrospinal fluid system. The selection of neurological material has been made judiciously, so that the ophthalmologist will find in the book the information necessary for the understanding of practically all the neurological diseases that he is likely to encounter. A bibliography containing over 1700 references and covering the last eight years is included.

In summary, Dr. Lyle's Neuro-Ophthalmology is intended to guide the ophthalmologist in all neurological matters. There is no doubt in the reviewer's mind that the book will serve well in that capacity.

PETER C. KRONFELD

ESCLERÓSES VALVULARES CALCIFICADAS: ESTUDO ANÁTOMO-PATOLÓGICO, RADIOLÓGICO E CLÍNICO, COM APRESENTACÃO DE CEM CASOS. By Dr. Roberto Menezes de Oliveria, Capitão Médico do Corpo de Saúde da Aeronáutica, Diplomado em Medicina de Aviação pela Diretoria de Aeronáutica do Ministério da Marinha, etc. Paper. Pp. 155, with 67 illustrations. Rio de Janeiro, Brasil: Tipografia do Patromato, 1943.

This monograph, carefully edited and well printed on high quality paper, is a worthwhile work. The author's analysis of the result of his investigation of one hundred cases of valvular calcification, encountered at the Peter Bent Brigham Hospital, in Boston, is well presented and each statement is based on abundant clinical, roentgenologic, pathologic and statistical proof. The relatively voluminous reports of cases are illustrated by about fifty well reproduced roentgenograms. In the text, the author mentions more than one hundred bibliographic references.

The author warns against the usually incom-

plete diagnoses in the field of his investigation. Concerning twenty-five of the cases of calcified annulus fibrosus, data derived from necropsy are given. Certain of the author's findings from this source and from his clinical studies are of particular interest. A purely degenerative process limited to the valve rings does not interfere with function whereas a process which results in calcification indicates a lesion of the valve. Calcified lesions of the aortic valvular region involve both ring and valves. The presence of calcification of the mitral valve is pathognomonic of mitral stenosis only when limited to the valve proper. Calcification of the annulus fibrosus of the mitral valve is one of the most frequent and earliest signs of arteriosclerosis. In rheumatic cases any calcification which extends to the valves proper indicates a functional valvular lesion. The degenerative signs found with cardiac degeneration associated with calcification include: coronary calcification (25 per cent); calcification of the aorta (20 per cent); hypertrophic changes in the vertebrae; cholelithiasis; hyperostosis of the skull; osteoporosis and Paget's disease, and kyphosis. Disturbance in calcium metabolism was present in 20 per cent of the cases. Predominance of the condition among females is explicable through the disturbance of calcium metabolism after menopause and the higher incidence of hypertension among women.

The six pages of methodically presented summary and conclusions are an invaluable part of the work. Besides being printed in the author's native Portuguese they also appear translated into English. The author concludes that roentgenologic studies of valvular calcification facilitate investigation of the following: (1) exact movements of cardiac valves; (2) movements associated with suction exerted by the base of the heart; (3) the importance of this latter movement in the determination of cardiac output, and (4) the fallacy of measuring cardiac output by registering the difference between systolic and diastolic silhouettes.

Great credit is due the author for the thorough manner in which he has handled his subject. This work should inspire further contributions on roentgenology of the heart, especially from Latin America.

SEBASTIÃO V. FRANCO

A BIBLIOGRAPHY OF AVIATION MEDICINE: SUPPLEMENT. By Phebe Margaret Hoff, Ebbe Curtis Hoff and John Farquhar Fulton. Cloth. Price, $2.50. Pp. 109. Published (1944) by the Committee on Aviation Medicine, Division of Medical Sciences, National Research Council, Acting for the Committee on Medical Research, Office of Scientific Research and Development, Washington, D. C. Distributed by Charles C Thomas, Springfield, Illinois.

This supplement is a continuation of the previous original Bibliography of Aviation Medicine compiled by Hoff and Fulton, and published in 1942. The present volume is made up of a list of 2,336 entries; these, with the references in the first volume, comprise a total of over 7,000 items devoted to this special field.

Despite the timely, and in fact imperative, interest in all matters pertaining to the aviator on account of war conditions, one would hardly believe that so many articles dealing with this subject could be published in such a relatively short time. An inspection of the volume, however, reveals at once how far reaching this field is and how many other interests are closely associated with aviation, especially in war time. For example, there is an added topic in this supplementary volume which deals with Survival and Rescue. References are found in this section which are concerned with such pertinent subjects as the effects of sea water on experimental animals, shark bite, points of interest in Navy fishing instructions, the effect of exposure on flyers to Arctic waters, etc., etc. The remarkable and dramatic story of the development of the Air Transport of the Sick and Wounded has been continued in the supplement by the addition of new references since the first publication in 1942.

In order that the reader may obtain some idea of the extent and nature of the bibliography, it should be stated that the material is divided into fourteen main topics, as follows: (1) History and General Aspects of Aviation Medicine, (2) The Special Physiology of Aviation and Conditions Simulating Flight, (3) The Special Pharmacology of Aviation and Conditions Simulating Flight, (4) The Special Psychology of Aviation and Conditions Simulating Flight, (5) Aeromicrobiology (Bacteriology and Immunology in Aviation and High Altitudes), (6) Diseases and Accidents in Aviation and Conditions Simulating Flight, (7) Selection and Assessment of Efficiency of Flight Personnel, (8) Training, Performance and Fatigue of

Flight Personnel, (9) Protection of Flight Personnel, Preventive Medicine and Therapeutics of Aviation, (10) Aviation and Public Health (Sanitary Aviation), (11) Organization of Aviation Medicine, (12) Special Problems, (13) General Studies in Aviation Medicine, and (14) Bibliographies.

This publication commands interest for several reasons: first, because it is a collection of bibliographical information about a new and special topic which is of immediate importance and growing interest; second, because it appears to be a model pattern for the presentation of medical bibliography; and third, because the publication is obviously more than a simple and accurate compilation of data. As the authors say, a classified bibliography to deserve its name, must preserve an "analytical function, else it becomes merely a sterile list of references." The reviewer is impressed with the care, the thought and the planning which have obviously been devoted to the selection, classification and arrangement of the material in this volume. It is to be hoped that other such carefully prepared bibliographies relating to medical topics will be available in the future. The collection and preparation of such data are not, however, a routine task to which the novice should be assigned for such work demands the mature and intelligent judgment of one experienced in the field. Any one who contemplates the preparation of such a collection would do well to peruse the work of Hoff, Hoff and Fulton and use it as an effective method of presentation.

C. C. Sturgis

BOOKS RECEIVED

Pediatric X-Ray Diagnosis: A Textbook for Students and Practitioners of Pediatrics, Surgery & Radiology. By John Caffey, A.B., M.D., Associate Professor of Pediatrics, College of Physicians and Surgeons, Columbia University; Associate Pediatrician and Roentgenologist, Babies Hospital and Vanderbilt Clinic, New York City, etc. Cloth. Price, $12.50. Pp. 838, with 711 illustrations. Chicago: Year Book Publishers, 1945.

Nutrition and Chemical Growth in Childhood. Volume II. Original Data. By Icie G. Macy, Ph.D., Sc.D., Director of the Research Laboratory, Children's Fund of Michigan. With a Foreword by Lawrence Reynolds, M.D., Editor of the American Journal of Roentgenology and Radium Therapy. And a Supplement by Julia O. Holmes, Ph.D. Cloth. Price, $10.00. Pp. 1027 (433–1460), with 706 illustrations. Springfield, Illinois: Charles C Thomas, 1946.

Whooping Cough. By Joseph H. Lapin, B. Chem., M.D., Adjunct Pediatrician, Bronx Hospital; Associate in Contagion, Riverside Hospital for Contagious Diseases, New York. Cloth. Price, $4.50. Pp. 238, with 40 illustrations. Springfield, Illinois: Charles C Thomas, 1943.

Pulmonary Tuberculosis in the Adult: Its Fundamental Aspects. By Max Pinner, M.D., Chief, Division of Pulmonary Diseases, Montefiore Hospital for Chronic Diseases, New York; Editor, *American Review of Tuberculosis:* Clinical Professor of Medicine, College of Physicians and Surgeons, Columbia University, New York. Cloth. Price, $7.50. Pp. 579, with 59 illustrations. Springfield, Illinois: Charles C Thomas, 1945.

The Dental Treatment of Maxillo-facial Injuries: With Supplementary Material on Cases and Techniques. By W. Kelsey Fry, M.C., M.R.C.S., L.R.C.P., L.D.S., R.C.S. (Eng.), Consulting Dental Surgeon to the Royal Air Force; Consulting Dental Surgeon to the Ministry of Health; Dental Surgeon to Guy's Hospital; P. Rae Shepherd, L.D.S., R.C.S. (Eng.), Dental Surgeon, East Grinstead Maxillo-facial Unit; Alan C. McLeod, D.D.S (Penn.), B.Sc. (Dent.), Toronto, L.D.S., R.C.S. (Eng.), Dental Surgeon, East Grinstead Maxillo-facial Unit; and Gilbert J. Parfitt, M.R.C.S., L.R.C.P., L.D.S., R.C.S. (Eng.), Dental Surgeon, East Grinstead Maxillo-facial Unit. With Foreword by Professor F. R. Fraser, M.D., F.R.C.P., Director General, Emergency Medical Service; and a Section on Fractures of the Middle Third of the Face by A. H. McIndoe, M.S., F.R.C.S., F.A.C.S., Consulting Plastic Surgeon to the Royal Air Force, Surgeon-in-Charge, East Grinstead Maxillo-facial Unit. Cloth. Price, $6.50. Pp. 434, with many illustrations. Philadelphia: J. B. Lippincott Company, 1944.

The Neurosurgical Patient: His Problems of Diagnosis and Care. By Carl W. Rand. Clinical Professor of Neurological Surgery, University of Southern California, School of Medicine, Los Angeles, California. Cloth. Price, $4.00. Pp. 576, with 121 illustrations. Springfield, Illinois: Charles C Thomas, 1944.

An Atlas of Anatomy. By J. C. Boileau Grant, M.C., M.B., Ch.B., F.R.C.S. (Edin.), Professor of Anatomy in the University of Toronto. In two volumes. Volume II. Vertebrae and Vertebral Column, Thorax, Head and Neck. Cloth. Price, $5.00. Pp. 390, with 460 illustrations. Baltimore, Maryland: Williams and Wilkins Company, 1943.

Dr. W. C. Röntgen. By Otto Glasser, Cleveland Clinic Foundation. Cloth. Price, $4.50. Pp. 169, with illustrations. Springfield, Illinois: Charles C Thomas, 1945.

François Magendie: Pioneer in Experimental Physiology and Scientific Medicine in XIX Century France. By J. M. D. Olmsted, Professor of Physiology, University of California. Cloth. Price, $5.00. Pp. 290, with illustrations. New York: Schuman's, 1944.

A Bio-Bibliography of Andreas Vesalius. By Harvey Cushing. Cloth. Price, $15.00. Pp. 229, with many illustrations. New York: Schuman's, 1943.

The Harvey Cushing Collection of Books and Manuscripts. Cloth. Price, $8.50. Pp. 207. New York: Schuman's, 1943.

Radiumdosimetrie. Von Dr. phil. Walter Minder, Technischer Leiter des Institutes der Bernischen Radiumstiftung in Bern. Cloth. Price, $5.50. Pp. 183, with 97 illustrations. Wien: Julius Springer, 1941. J. W. Edwards, Publisher, Ann Arbor, Michigan.

Siebzehn Jahre Strahlentherapie der Krebse. Zurcher Erfahrungen 1919–1935. Von Hans R. Schinz und Adolf Zuppinger. Cloth. Price, $11.75. Pp. 340, with 95 illustrations and 213 tables. Leipzig: Georg Thieme, 1937. J. W. Edwards, Publisher, Ann Arbor, Michigan. (This book has already been reviewed in the American Journal of Roentgenology and Radium Therapy, 1938, *40*, 778.)

Kurzwellentherapie. Von Dr. Josef Kowarschik, Professor für physikalische Therapie an der Universität Wien. Third edition. Cloth. Price, $4.25. Pp. 143, with 138 illustrations. Wien: Springer, 1943. J. W. Edwards, Publisher, Ann Arbor, Michigan.

Röntgenphysik. Von Dr. med. Adolf Liechti, Professor für medizinische Radiologie; Direktor des Röntgeninstitutes der Universität Bern. Mit Beiträgen von Dr. phil. Walter Minder, Technischer Leiter des Institutes der Bernischen Radiumstiftung. Cloth. Price, $11.75. Pp. 308, with 227 illustrations. Wien: Julius Springer, 1939. J. W. Edwards, Publisher, Ann Arbor, Michigan.

Ultraviolette Strahlen: Ihre Erzeugung, Messung und Anwendung in Medizin, Biologie und Technik. Von A. E. Herbert Meyer, Dr. phil., and Ernst Otto Seitz, Dr. phil. Mit einem Geleitwort von Professor Dr. B. Rajewsky, Direktor des Kaiser-Wilhelm-Institutes für Biophysik, Frankfurt a. M. Cloth. Price, $10.00. Pp. 308, with 217 illustrations and 40 tables. Berlin: Walter de Gruyter & Co., 1942. J. W. Edwards, Publisher, Ann Arbor, Michigan.

Ultrakurzwellen in ihren medizinisch-biologischen Anwendungen. Von H. Dänzer, H. E. Hollmann, B. Rajewsky, H. Schaefer and E. Schliephake. Cloth. Price, $8.40. Pp. 308, with 188 illustrations and 24 tables. Leipzig: Georg Thieme, 1938. J. W. Edwards, Publisher, Ann Arbor, Michigan.

Invisible Radiations of Organisms. By Otto Rahn, Professor of Bacteriology, Cornell University. With an Introduction to the Physics of Radiation. By Sidney W. Barnes, Research Associate in Physics, University of Rochester. (Protoplasma-Monographien, Volume 9.) Cloth. Price, $4.75. Pp. 215, with 52 illustrations. Berlin: Gebrüder Borntraeger, 1936. J. W. Edwards, Publisher, Ann Arbor, Michigan.

DEPARTMENT OF TECHNIQUE

Department Editor: ROBERT B. TAFT, M.D., B.S., M.A., 103 Rutledge Ave. Charleston, S. C.

A DEMONSTRATION ROENTGEN-RAY MACHINE "LIVE" CIRCUIT-DIAGRAM MODEL*

By LIEUTENANT COLONEL LINNEUS G. IDSTROM,**
CAPTAIN HERBERT LANGFORD,† *and*
TECHNICAL SERGEANT WALLACE P. BAKER‡

NUMEROUS training aids have been devised for the study of roentgen machines and their electrical circuits. We are aware of demonstration types of roentgen machines used for these purposes. One of us has had the opportunity of using and becoming familiar with the training board used at the Army School of Roentgenology and the electric model of a roentgen machine constructed by Williams[1] and in use at the Mayo Foundation.

The demonstration apparatus used at the Army School of Roentgenology is of wall-display type and produces roentgen rays. The electric model in use at the Mayo Foundation is constructed from radio parts including radio rectifier tubes for demonstration of rectifying circuits, their resultant wave forms and their effect on the quantity and quality of the radiation produced. This model functions at low voltage and was constructed primarily to demonstrate basic principles of roentgen machines and common types of rectifying circuits.

Incorporating the methods of teaching already successfully used in Army Signal Corp Schools, we have designed a roentgen machine (Fig. 1 and 2) with a "live" diagram-circuit broken down into teaching units, divided as follows:

Autotransformer unit	(Fig. 1, No. 1—yellow)
High voltage transformer unit	(Fig. 1, No. 2—red)
Rectifier units	(Fig. 1, No. 3—blue)
Full-wave rectification unit (bridge rectifier)	(Fig. 1, No. 3A—blue)
Half-wave rectification unit	(Fig. 1, No. 3B—blue)
Self-rectification unit	(Fig. 1, No. 3C—blue)
Control circuit unit	(Fig. 1, No. 4—orange)
Filament circuit unit	(Fig. 1, No. 5—gray)
Roentgen tube unit	(Fig. 1, No. 6—green)
Oscilloscope	(Fig. 1, No. 7—separate unit)
Hand timer	(Fig. 1, No. 8—accessory)

Actual parts are shown on the panel and are all integral working parts of the "live" circuit except the "high tension" transformer, details of which will be mentioned later. Certain parts are included behind the panel and incorporated within the circuit behind the board to produce desired results as expected from the basic exterior demonstration diagram.

Our circuit is so designed that three machines can be demonstrated readily: full-wave rectifier with 100 ma., "100 kv." (peak) (Fig. 1, 3A); half-wave rectifier with 60 ma., "100 kv." (peak) (Fig. 1, 3B, Fig. 2, 3B); and self-rectifier 30 ma., "100 kv."

[1] Williams, M. M. D. Electric model of an x-ray machine. *Radiology*, 1942, *38*, 338–349.

* Constructed at Central Signal Corps School, Camp Crowder, Missouri.
** Medical Corps, Army of the United States.
† Signal Corps, Army of the United States.
‡ Medical Department, Army of the United States.

(peak) (Fig. 1, 3c, Fig. 2, 3c). Within limits, these machines are operated much like an ordinary roentgen machine. As safety factors, production of actual high tension voltage and development of roentgen rays are eliminated as unnecessary.

Primary circuit voltages, kilovoltage, and milliampere measurements are readily visualized in approximately correct meter readings. A gas-filled rectifier (tungar rectifier with base removed) is chosen as the "roentgen tube" because rectified current is produced, filament changes result in visual proof of milliamperage change, the photoelectric effect of electron emission is demonstrable, and the tube is similar in appearance to a roentgen tube with cathode and anode visible (Fig. 1, No. 6).

Through the use of an oscilloscope (Fig. 1, No 7), voltage wave form, including rectification, is shown in various parts of the circuit. By connecting a 100 to 200 ohm resistor into the "high tension" circuit, milliamperage wave forms are studied. (We have used 3 inch and 7 inch oscilloscopes, the former for classroom demonstrations; the latter for larger groups.)

THE CIRCUIT

The design, in which a standard simplified circuit is broken down into six subdivisions, already enumerated, allows in panel 3 (Fig. 1) a substitution of the three types of rectification units without disturbing the remainder of the circuit. The other panels are thus kept in a fixed position.

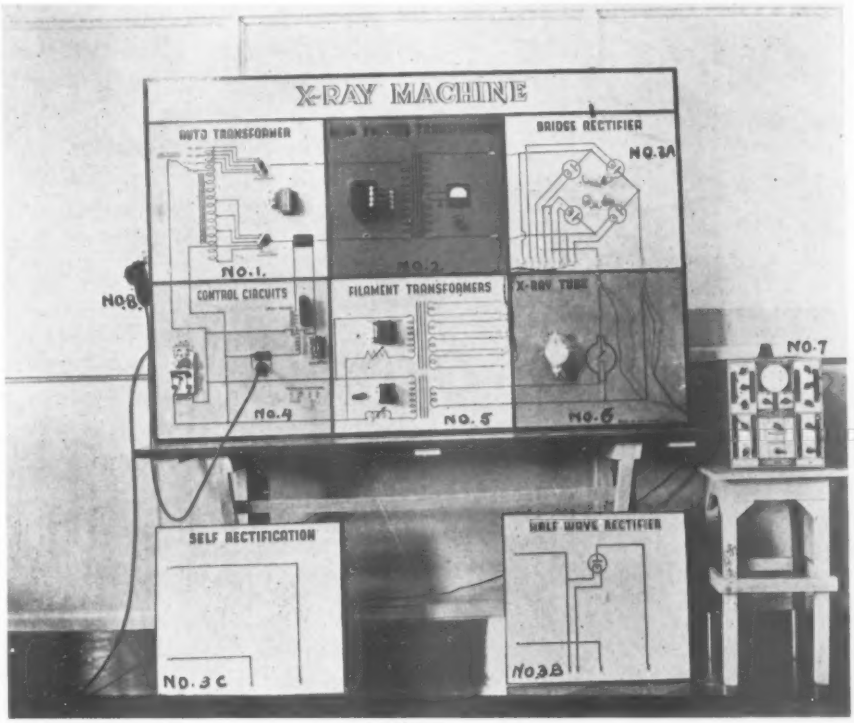

Fig. 1. Demonstration roentgen-ray machine. Full-wave rectification panel in circuit.

The machine is constructed on a 6 by 4 ft. board mounted vertically and supported on a shelf 18 inches wide, the latter also serving as a counter for holding plug-in wires, resistors, and other associated training aids. Allowing for a 6 inch panel across the top for title, the board is divided into six units, plus two substitution units, each section measuring 21 by 24 inches. Panels

are painted a different color for better visualization of each unit. The circuit diagram is painted on the board in solid black lines as seen in Figure 1.

AUTOTRANSFORMER UNIT

The upper left hand panel (painted yellow) contains the autotransformer (Fig. 1, No. 1) hand wound, using the core of a small radio transformer. Taps are brought out to give secondary voltages ranging from 50 to 150 volts. Major tap controls allow for 20 volt gradations and minor tap controls for 5 volt changes. On the primary side of the autotransformer, line voltage compensation is effected through 100, 110, 120 and 130 volt taps.

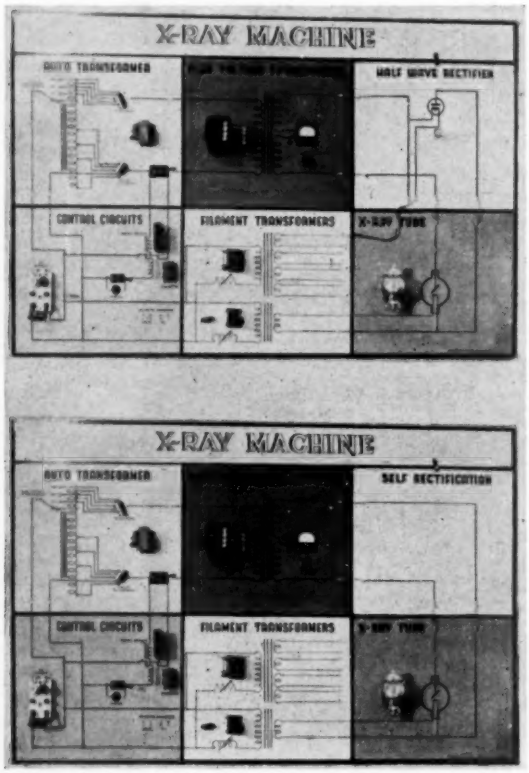

FIG. 2. Demonstration roentgen-ray machine showing half-wave rectification panel (*A*) and self-rectification (*B*) as part of circuit. (*A*, above; *B* below.)

The leads from the autotransformer (Fig. 3) are seen behind the board, with the fixed primary lead connected to one side of the A.C. line coming from the control circuit unit. The four primary tap leads (line voltage compensation) connect to snap fasteners on the board. The other A.C. line lead is also brought to the front surface of the board and terminates in a snap to fit any one of the snap fasteners of the primary taps.

Secondary taps for the major adjustments are connected to a five-position wafer switch. Switch and leads are mounted behind the board with control knobs placed on the surface of board over the painted taps of the diagram. Minor control taps are similarly connected behind the board. The two leads from the common points on the wafer switches are connected to snap fasteners at the right edge of this panel, the lower also incorporating a knife switch for manual timing. The control unit can thus be excluded from the circuit.

By the method described, the painted diagram is incorporated into the circuit through live snap fastener taps which are available on the front side of the board. Each unit is similarly constructed in this regard.

HIGH VOLTAGE TRANSFORMER UNIT

The second panel (Fig. 1 and 2, No. 2) should normally include a functioning high tension transformer. The use of a training aid by inexperienced personnel (enlisted men and WAC trainees in our department) precluded the use of dangerous voltages. Therefore, this panel (painted red) shows the schematic diagram of a high voltage transformer. The transformer mounted on this section, however, is a "dummy" with the case made from the end of a pressed-meat can (painted black) and four stand-off insulators. Realism is obtained by running two "low voltage" (dummy) leads into the transformer case through rubber grommets and running four "high voltage" (dummy) secondary leads from the stand-off insulators to four similar high tension insulators on the display panel (see Fig. 1).

The meter (Fig. 4), also mounted on this

panel in the conventional manner, is shown grounded at zero potential in the secondary circuit. Through the use of a three-pole, three-position switch, the meter does triple duty, serving to record volts, "kilovolts" and milliamperes. As a milliameter (first position of switch—ma.) it is actually mounted directly in the circuit between the simultaneously connects the leads from the knife switch (autotransformer panel) to the rectifier panel, thus restoring the circuit that is otherwise broken as the milliammeter is removed. The 2000 ohm resistance will permit a full scale deflection of 200 volts, the face of the meter being calibrated accordingly.

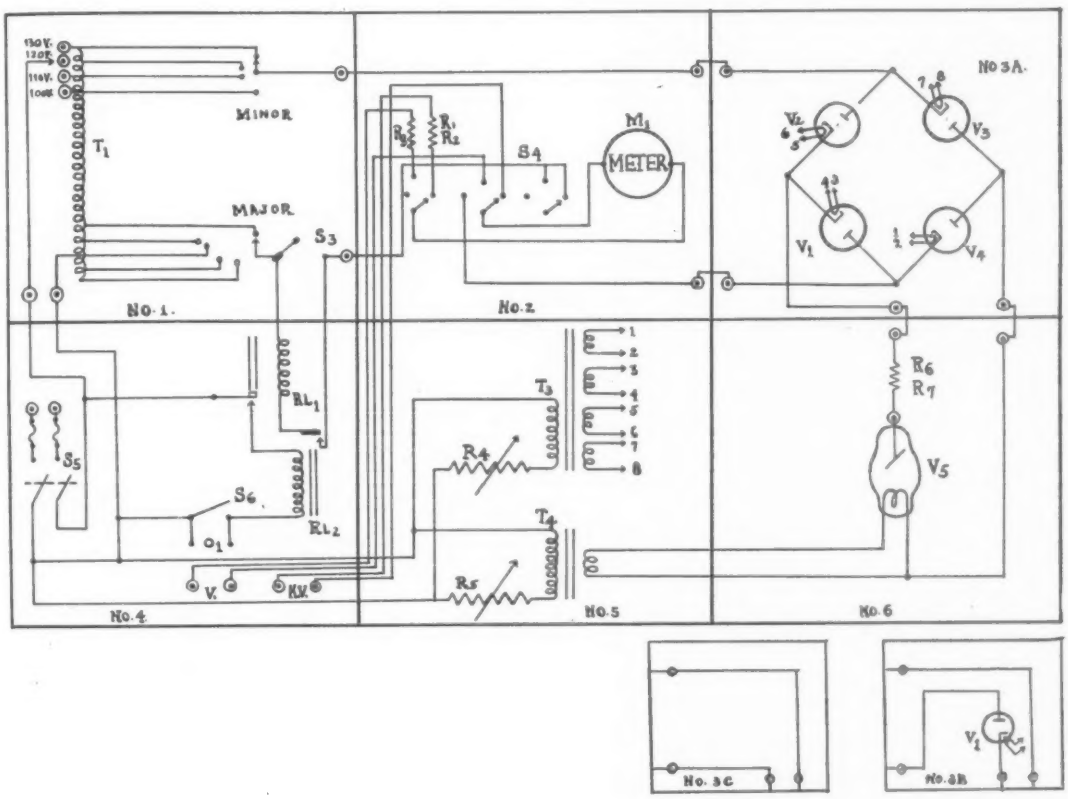

FIG. 3. Diagram of a circuit as actually found on back side of demonstration board with full-wave rectification panel (No. 3C) inserted. Substitution panels for half-wave rectification (No. 3B) are shown in smaller diagrams below. See Figure 4 for detail of all-purpose meter diagram (No. 2).

autotransformer and the rectifier (see Fig. 2) and is shunted (by an internal shunt) to read 100 ma. at full-scale deflection.

By turning the selector switch to the second position (volts) the meter is connected through a 2000 ohm resistor to the volts terminals on the control circuit panel (Fig. 1, No. 4) This outlet allows for its incorporation into the primary or control circuits for voltage measurements at any snap-fastener connections. The selector switch

The third position of the selector switch ("kv.") connects the meter through a 1500 ohm resistance to the ("kv.") terminals on the control circuit panel. The 1500 ohm resistance will result in a full scale deflection of 150 volts but the face of the scale is not so calibrated. The maximum output of the autotransformer (with line voltage compensation taps correctly set) is 150 volts, and this voltage connected to the kilovolt terminals will give a full meter

scale deflection. If the machine had an actual high tension transformer, the high tension equivalent of 150 volts on the autotransformer would be 100 kv. on the secondary circuit. Therefore, a meter scale 0-100 is used as the kilovolt scale. Thus, voltmeter leads taken from the high tension side of the high voltage transformer and connected to the kilovolt taps will read a fictitious peak of 100 kv. for 150 peak volts of primary and proportionately lesser "kilovolts" when tapped down through major and minor controls (secondary circuit of autotransformer).

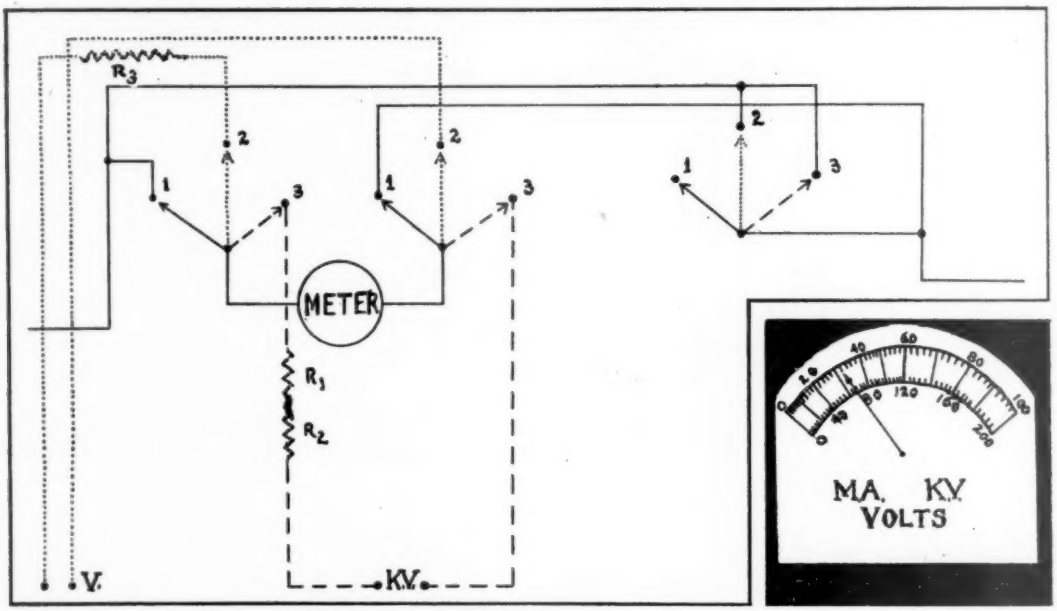

FIG. 4. Detailed diagram of circuit using an all-purpose meter (see insert) with a three-hole, three-position switch. Milliamperage is recorded with switch in position 1, voltage in position 2, and kilovoltage in position 3. Voltmeter and kilovoltmeter terminals are seen in control panel (Fig. 1 and 3, No. 4).

RECTIFIER CIRCUIT UNITS

The third panel, painted blue (Fig. 1, No. 3, A, B or C), contains the rectifier circuit in which the versatility of the board is increased. As mentioned earlier, simple demonstration of various types of rectification is done by making interchangeable panels. The *self-rectification* panel (Fig. 1, No. 3C) is used for demonstration of the Army portable self-rectifying roentgen unit in its basic form. Wiring is carried directly through from high voltage transformer to the roentgen tube. By replacing this panel with the *half-wave rectifier* panel (Fig. 1, No 3B) a circuit incorporating a single radio tube rectifier is made possible. By inserting a third panel (Fig. 1, No. 3A) a *full-wave rectifier* becomes an integral part of the circuit. This unit demonstrates the usual type of permanent installation seen. By removing one valve tube from this circuit, the oscilloscope also shows the change from full-wave to half-wave rectification, which occurs with loss of one or both tubes which are paired in series in the full-wave (bridge) rectifying circuit.

CONTROL CIRCUIT UNIT

The *control circuit* (Fig. 1, No. 4), painted orange, contains the following essentials: main switch (double pole, single throw) and fuses connected to 110 volt A.C. outlet, contactor, circuit breaker, knife switch for manual circuit closure, outlet for attachment of timer obtained from regular portable roentgen machine, and voltage and "kilovoltage" meter connections.

The knife switch is incorporated to demonstrate a simple timer device. A similar knife switch is found in the autotransformer circuit (Fig. 1, No. 1) functioning as a manual timer when the control circuit timer switch is open, demonstrating timing as it was performed in the roentgen unit used in World War I.

The contactor and circuit breaker readily show their protective value with demonstration of line surges and "short circuits."

The control circuit is thus an aid in demonstration of refinements seen in present-day machines.

FILAMENT TRANSFORMER UNIT

The *filament transformer unit* (Fig. 1, No. 5), painted gray, contains a small step-down transformer for supplying current to the "roentgen" tube filament. The filament control is on the panel and governs a small rheostat (illustrated as a choke coil).

For convenience, a step-down transformer with four identical secondary windings supplies the filaments of the rectifier tubes. This is a slight variant from the more common use of two similar step-down transformers each functioning to supply the filament of a valve in the bridge rectifier and a third step-down transformer for the filaments of the remaining two-valve tubes. A control for valve tube filaments is also available on the front side of the panel but it is not turned conveniently without pliers. This control (also a rheostat) so arranged demonstrates the need for occasional filament control of valve tubes for maximum tube life and efficiency.

ROENTGEN TUBE UNIT

The roentgen tube unit consists only of the roentgen tube which in this model is a tungar rectifier with base removed. No increase in demonstration value would result from use of a real roentgen tube whereas definite bodily harm might be incurred through production of high voltage and actual roentgen rays. Certain advantages are offered through the use of a gas-filled tube. The tungar rectifier has an appearance quite similar to a basic roentgen tube. Filament control is readily visualized and the photoelectric effect of electron emission is effectively demonstrated when the timer switch is closed. With the insertion of resistors in the "high tension" circuit (Fig. 2, No. 6) both voltage and milliamperage waves are demonstrable on the oscilloscope.

To all intents and purposes, the tube used therefore adequately demonstrates a real roentgen tube and has the advantage of safety factors mentioned.

SUMMARY

A model is so constructed that the use of a "live" circuit-diagram is incorporated with the fundamental working parts of a basic roentgen machine (high voltage transformer excepted). Through the use of snap-fastener connections at all important points, the diagram is "live" electrically for the demonstration of fundamental teaching problems.

The circuit is divided into basic units through the use of colored panels. Circuit connections can be varied between panels. For further versatility, the rectifier panels are interchangeable, resulting in a teaching aid with three or more demonstrable types of roentgen machines.

We believe that this demonstration roentgen machine will prove of value in other army and civilian hospitals and teaching centers. It is of simple construction and many parts can be obtained from old radio or electrical equipment. Other parts can be designed and built to fit the needs of the machine.

Lieut. Col. L. G. Idstrom
Grays Bay
Wayzata, Minn.

EQUIPMENT DATA

M_1 —100 ma. meter (also used as voltmeter and "kilovoltmeter")

O_1 —Standard two-pole convenience outlet

R_1, R_2 —750 ohm-5 watt resistors (equivalent to one 1500 ohm-10 watt resistor)

R_3 —2000 ohm-12 watt resistor

R_4 —500 ohm-50 watt potentiometer with knob control
R_5 —500 ohm-50 watt potentiometer with screw control
R_6, R_7 2500 ohm-12 watt resistors
S_1, S_2 —Five position wafer switches
S_4 —Three pole-three position wafer switch
S_3, S_6 —Single pole-single throw knife switches
S_5 —Double pole-single throw fusable knife switch
T_1 —150 volt autotransformer (see winding data)
T_2 —High voltage transformer (dummy)
T_3 —Filament transformer for rectifier tubes (see winding data)
T_4 —Filament transformer for simulated roentgen tube (see winding data)
RL_1 —Circuit breaker
RL_2 —Contactor
V_1, V_2, V_3, V_4 —Vacuum tube rectifiers, type IV.
V_5 —Simulated roentgen tube (tungar rectifier with base removed)
Snap fasteners
Power cord and plug
Switch and rheostat knobs
Lugs for soldered connections
Copper hook-up wire
Miscellaneous nuts and bolts
Two pairs of meter leads with snap tips
Two pairs of oscilloscope leads with snap tips
Oscilloscope (separate unit)
Hand timer (separate unit)

Each transformer is wound to fit the specific plans for a demonstration machine. Wire sizes are not too important, and like most other parts, are dependent upon what is available.

The autotransformer (T_1) was constructed from core and shell of a "burned out" 40 watt radio filament transformer.

Winding procedure: No. 30 enameled copper wire (a larger size may be used) is wound—four turns per volt—with taps brought out as follows: (1) start; (2) 80 turns; (3) 160 turns; (4) 240 turns; (5) 320 turns; (6) 480 turns; (7) 520 turns; (8) 540 turns; (9) 560 turns; (10) 580 turns; final tap at 600 turns. Of these, five are used as primary taps and ten as secondary taps so it is seen that four taps do double duty. This is accomplished by connecting one side of the A.C. supply to tap (2) and *not* to tap (1). The other side of the A.C. supply is fitted with a snap fastener which is connected to tap (11) for 130 volts line voltage; to tap (9) for 120 volts; to tap (7) for 110 volts; and to tap (6) for 100 volts. Taps (1), (2), (3), (4), and (5) are connected to the five positions of the major adjustment switch. Taps (7), (8), (9), (10), and (11) are connected to the minor adjustment switch.

With the primary line voltage compensation (primary taps) set to corresponding line voltage, it is possible to vary secondary voltage from 50 to 150 volts in five volt steps.

The *filament voltage transformer* (T_3) for the rectifier tubes is wound to the following specifications:

Core and shell—salvaged from a small radio filament transformer with a "burned out" secondary (here again a 40 watt transformer is satisfactory).

Primary winding—used without modification.

Secondary winding—The old secondary winding is carefully removed and turns are counted. From these data and secondary voltage rating it is determined that the turns per volt should be 5.5. Then four identical secondary windings are wound over the primary using 40 turns of No. 22 enameled copper wire for each winding.

This results in a voltage slightly above the 6.3 volt rating of the 1 *V* tubes but this voltage could be dropped by means of resistance R_4 (Fig. 2). Separate leads are brought out from each secondary winding.

Turns per volt will vary with type of transformer obtainable.

The *filament voltage transformer* (T_4—Fig. 2) for the simulated roentgen tube is wound in a manner similar to that used in winding transformer T_3. In this instance, however, the turns per volt figure is 5.0 for the single secondary coil wound.

Secondary winding—The secondary is wound with a pair of No. 14 enameled copper wires to insure enough current capacity.

(A single No. 12 or larger enameled copper wire would be satisfactory to supply the 15 amperes drawn by the tungar rectifier but No. 14 wire is more easily wound then either No. 12 or No. 10 wire.) The winding is made with 12 turns which give an output of 2.4 volts with 120 volts on the primary side. Secondary voltage is controlled by R_5 (see Fig. 2).

A PORTABLE VIEWING BOX AND DISPLAY CASE

By MILTON S. LLOYD, M.D.
NEW YORK, NEW YORK

THE piece of equipment described below performs a double function without loss of efficiency for either purpose.

As a roentgen-ray viewing box, it accommodates six 14×17 inch films or an equivalent surface area of smaller ones. As a display case, it provides space for one hundred standard lantern slides or four hundred 35 mm. mounts or any desired combination of the two. As part of a physician's office furniture, one-half may be used as a roentgen-ray viewing box and the other half for an exhibit of interesting

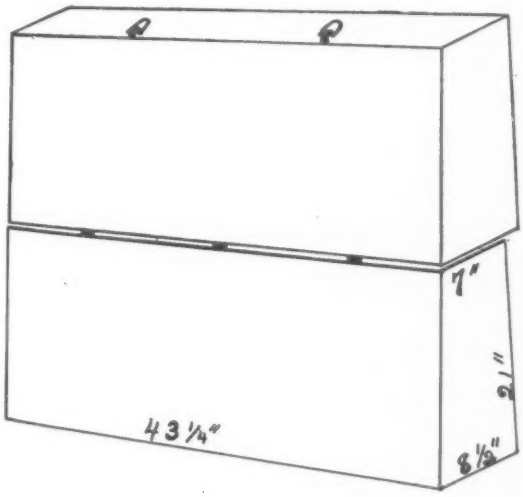

FIG. 1. This shows the outline with measurements in inches.

or attractive transparencies. In this way, it is useful and decorative at the same time.

Since its construction is not beyond the ability of any good workman, the rough blueprint data are provided herewith. The box measures $43\frac{1}{4}\times21\times15\frac{1}{2}$ inches and is made of $\frac{3}{4}$ inch lumber, preferably of light weight. It is placed in such a position that the $15\frac{1}{2}\times43\frac{1}{4}$ inch surfaces form the top and bottom. Then it is cut lengthwise on the bias leaving, on the top, a 7 inch strip at the back and an $8\frac{1}{2}$ inch strip at the front. On the bottom, the strips are of equal dimension, but reversed in position. Three hinges are then provided for the top and a pair of strong clasps for the bottom. Two struts are fitted to the bottom so as to project 5 inches beyond the edge at the back. They should be attached by a single large screw or bolt, so that they can be swung under for the sake of portability. When the box is opened, it presents a plane front $42\frac{1}{4}\times43\frac{1}{4}$ inches sloping backward, a total of 3 inches from the vertical.

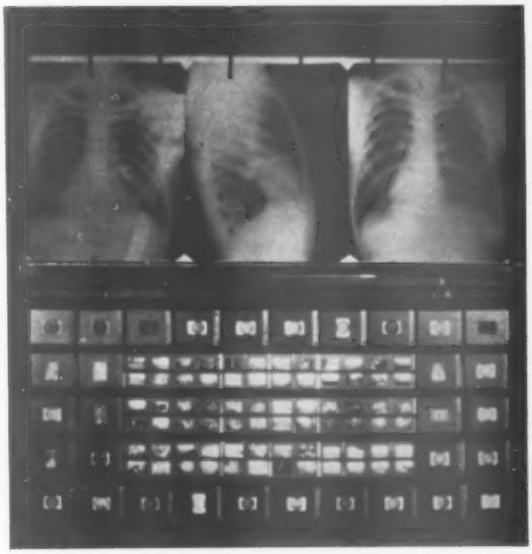

FIG. 2. A photograph of the case being used as a viewing box in the upper section and as a permanent exhibit of Kodachromes in the lower.

The entire box is painted white on the inside. Each half is measured off in three equal sections and, in each section is installed a pair of sodium vapor lights of 15 watt strength and 18 inches long. The lights are backed by a continuous sheet of metal, shaped to form a curved reflector for each pair. The metal surface is then painted white. Detailed data for the installation of the lights and reflectors are not given, since they can be obtained from

any standard modern roentgen-ray viewing box.

A framework of supports is affixed and the enclosure is completed by a single sheet of triple-flash opalescent glass for each section.

A removable holding frame and panel is built for each section. The frames are provided with suitable springs on the upper borders to hold roentgenograms in position. The panels consist of six grooved strips laid upon cross pieces so as to accommodate five rows of ten standard lantern slides each—a total of one hundred for the two sections. If 35 mm. film is to be used, four exposures can be mounted between a pair of standard cover glasses. The lantern slides are inserted by sliding them along the grooved channels from the left hand end, and the entire panel, when thus set up, may be inserted into its proper section instead of the roentgen film holding frame. It is secured by wing buttons. The case may then be closed and the prepared exhibit easily transported by automobile without danger of breakage. In order to set it up, it is only necessary to open the case and plug into a source of electricity.

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INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Skeletal System

Bianchi, A., and Muscolo, D.: Lymphosarcomatosis with bone lesions 234

Pavlovsky, A., Paterson Toledo, R., and Muscolo, D.: Lymphogranulomatosis of bone 234

Brocklebank, J. A.: Focal osteitis fibrosa of the skull 235

Follis, R. H., Jr., and Jackson, D. A.: Renal osteomalacia and osteitis fibrosa in adults. 235

Gunther, L., et al.: Metabolism of bone salts in resistant rickets 235

Follis, R. H., Jr., et al.: Prevalence of rickets in children between two and fourteen years of age 236

Kuhn, H. H., and Hemphill, J. E.: Baker's cyst 236

Hauch, P. P.: Pneumoröntgenography of knee joint 237

Marottoli, O. R.: Fractures of external tuberosity of astragalus 237

Shearer, W. S.: Ainhum 237

General

Baylin, G. J.: Body section roentgenography. 238

Valls, J. E., and Schajowicz, F.: Hematogenous muscle tuberculosis 238

Colvin, S. H., Jr., Gore, I., and Peters, M.: A case of histoplasmosis (Darling) with autopsy 238

ROENTGEN AND RADIUM THERAPY

Kaplan, I. I.: One year observations of treatment of cancer with avidin (egg white) ... 239

Bean, W. B., Spies, T. D., and Vilter, R. W.: Note on irradiation sickness 239

Lederman, M., Clarkson, J. R., and Mayneord, W. V.: Rectangular teleradium fields 240

Goin, L. S.: Low-voltage contact irradiation therapy 240

Butler, C.: Cancer of the breast 240

Puente Duany, N., Canizares, R., and Fonts Abreu, E.: Cancer of the breast ... 241

Carvalho, N.: Cancer of the breast 241

Guzman, L.: Treatment of cancer of the breast and its results 242

Frangella, A.: Roentgen irradiation of cancer of the breast 242

Caprio, G.: Radio-surgical treatment of cancer of the breast 242

Terrizzano, M. F., and Terrizzano, A. J. M.: Castration in the radiation treatment of tumors of the breast 243

Cifarelli, F. P., and Pujadas, A. A.: Results of roentgen treatment of cancer of the breast 243

Binnie, G. G.: Regression of tumours following treatment by stilboestrol and x-ray therapy 243

McNattin, R. F.: Treatment of osteogenic sarcoma with preoperative roentgen radiation in large doses 244

Livingstone, J. L., et al.: Treatment of carcinoma of the lung 244

Douglas, S. J.: Cancer of the lip 245

Kaplan, I. I.: Hemangioma of the elbow successfully treated with radium at an early age 246

Beilin, D. S.: Clinical features, diagnosis, and treatment of carcinoma of colon and rectum 246

Melbin, M., and Stenstrom, K. W.: Results of treatment of 173 cases of carcinoma of rectum 246

Borak, J.: Theories on effectiveness of roentgen therapy in inflammatory conditions.. 247

Pool, H. H.: Roentgen therapy with low dosage in suppurative infections 247

Freireich, K.: Radiation therapy for obstructing tuberculous hilar lymph nodes.. 247

MISCELLANEOUS

McCaw, W. W.: Training of x-ray technicians at the School for Medical Department Enlisted Technicians 248

Rogers, G. L.: Instantaneous stereography.. 249

Morgan, R. H.: Reciprocity law failure in x-ray films 249

Ellis, F., and Miller, H.: Use of wedge filters in deep x-ray therapy 249

Spencer, R. R.: Place of National Cancer Institute in the cancer problem 249

Paterson, E.: Time-intensity factor in x-ray irradiation. Part I. Influence of overall time 250

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

SKELETAL SYSTEM

BIANCHI, ANDRÉS, and MUSCOLO, DOMINGO. Limfosarcomatosis con lesiones óseas. (Lymphosarcomatosis with bone lesions.) *Rev. ortop. y traumatol.*, Oct., 1943, *13*, 79–94.

Virchow in 1864 differentiated lymphosarcomatosis from the large group of leukemias but he also included malignant granuloma under this name. Kundrat in 1893 differentiated it from lymphogranulomatosis. By changing Virchow's name of lymphosarcoma to lymphosarcomatosis he defined its systemic character. Sternberg made a careful histopathological study of lymphosarcomatosis and established the differences between it and the leukemias and also between it and the true malignant tumors.

The disease generally begins in Waldeyer's lymphatic ring or in the mediastinal or retroperitoneal glands. It affects a whole group of glands from which it extends directly by propagation or more rarely by way of the lymphatic to other glands. The capsule soon breaks down and the glands become adherent to each other. All the surrounding tissues are infiltrated. The spleen is not affected and though the liver is involved the lesions are never so great as in lymphadenosis, which is an important differentiating sign. The vessels are surrounded and compressed but rarely infiltrated. The kidney is frequently affected and greatly enlarged.

A case is described in a young man seventeen years of age who first came for treatment for swelling of the submaxillary glands; the process extended to the mediastinal, abdominal and inguinocrural glands and to various bones. It was extremely malignant and the patient died in less than a year. Photographs, roentgenograms and microphotographs of the histopathological findings are given. The nodules in the kidneys and the tissue which surrounded the vena cava showed, as usual, that the lymphosarcomatosis had infiltrated the tissues without causing the destruction characteristic of malignant tumors. The process had spared the glomeruli and renal vessels as well as the vena cava. The compression of this vessel with marked reduction in its lumen had caused the great edema of the lower limbs.

Roentgen treatment was given and the growths proved very radiosensitive but the process was so diffuse that it could not be arrested permanently.—*Audrey G. Morgan.*

PAVLOVSKY, ALFREDO, PATERSON TOLEDO, R., and MUSCOLO, DOMINGO. Linfogranulomatosis ósea; comentarios sobre 25 observaciones. (Lymphogranulomatosis of bone; comment on 25 cases.) *Rev. ortop. y traumatol.*, Jan., 1944, *13*, 136–157.

Malignant lymphogranuloma or Hodgkin's disease is a pseudoleukemic disease belonging to the group of granulomas. It is generally classified as local or generalized but the authors use a classification into tumoral, infectious and mixed forms.

Sometimes the bones are involved. Among 402 cases seen by the authors there was bone involvement in 25, or 6.21 per cent. Occasionally the bone symptoms are primary. This was true in 4 of these cases. In all these the bone lesions were located in the sternum and biopsy material was obtained by puncture. It is probable that bone lesions are not visible roentgenologically at first as autopsy material shows a much larger proportion of bone lesions than does roentgen examination.

In 40 to 48 per cent of these cases bone involvement was a premonitory sign of death, but the authors believe that this is because the bone lesions usually appear late rather than that they add to the malignancy of the disease. However, in 3 cases the appearance of the bone lesions coincided with a change of the disease from a tumorous into an infectious form, with frank acceleration of malignancy and the beginning of cachexia. Various bones were involved in this series but the most frequent involvement is in the lumbar column and pelvis or the dorsolumbar column and ribs. In 2 of the cases the lymphogranulomatosis was associated with tuberculosis, in 1 case with Pott's disease and in the other with pulmonary and gland tuberculosis.

The roentgen characteristics of the bone

disease are discussed and illustrated with many roentgenograms of the different forms. A table is given showing the clinical features of the cases.

In the early tumoral stage, roentgen treatment is very effective but when the disease has taken on an infectious character it is ineffective.

In spite of the severity of the involvement of the vertebrae in some cases, the spinal cord and nerve roots are rarely affected; they were involved in only 4 of this series of cases. When the cord is affected it is generally by pressure from extrameningeal tumors rather than by infiltration of the meninges and cord.—*Audrey G. Morgan.*

Brocklebank, J. A. Focal osteitis fibrosa of the skull. *Brit. J. Radiol.*, Feb., 1944, *17*, 62–63.

A man of twenty-eight came for examination on account of headaches and an asymmetrical swelling of the face. He said the asymmetry and swelling in the right zygomatic region had been present as long as he can remember but in the last six months there had been a marked increase in size. His general health was good and the rounded tumor of the right cheek had displaced the eye upward and the corner of the mouth downward. There were similar tumors in the right temple and occiput, all painless. His facial appearance suggested trigeminal palsy on the right side but there was no muscular weakness nor disturbance of vision.

Roentgen examination showed dense sclerosis of the basal bones and great hyperostosis of the frontal, occipital and right parietal regions and the right maxilla. The whole of the skull showed many woolly patches which suggested osteitis deformans. There were cystic lesions in the pelvis and femurs.

Major J. Duncan White said that this was apparently a case of osteitis fibrosa. The cystic areas resembled those seen in hyperparathyroidism but this disease generally occurs in elderly women and this patient had no clinical symptoms of excessive endocrine activity. Quite frequently in osteitis fibrosa there is thickening of the vault of the skull which sometimes greatly resembles that seen in osteitis deformans.—*Audrey G. Morgan.*

Follis, Richard H., Jr., and Jackson, Deborah A. Renal osteomalacia and osteitis fibrosa in adults. *Bull. Johns Hopkins Hosp.*, April, 1943, *72*, 232–241.

This report concerns the autopsy findings in the vertebrae of 39 patients who died of renal insufficiency. The authors found that approximately 50 per cent of these patients had skeletal lesions. The most predominant finding was the presence of excessive osteoid tissue, justifying a diagnosis of osteomalacia; in a lesser proportion the changes of osteitis fibrosa cystica were found. The lesions were present more often in cases of chronic glomerulonephritis or pyelonephritis than in chronic vascular nephritis. They attempt no explanation of these skeletal changes because of the complexity of the problem and the difficulty in correlating such variable factors as blood serum protein, calcium and phosphorus, and the influence of the parathyroid hormone.

They refer to reports by Ginzler and Jaffe, Bergstrand, and Mach and Rutishauser that one can recognize histological alterations in the skeletal system of adults having renal insufficiency before they manifest themselves clinically or by roentgenological studies, but do not present evidence to support or disprove this contention.—*Angus K. Wilson.*

Gunther, Lewis, Cohn, Elma T., Cohn, Waldo E., and Greenberg David M. Metabolism of bone salts in resistant rickets; report of a case, with balance and radioactive studies. *Am. J. Dis. Child.*, Nov., 1943, *66*, 517–527.

This paper is the report of an investigation of the fate of labeled radioactive phosphorus and of the total calcium, magnesium and phosphorus balance in a case of intractable rickets. The patient was a boy who suffered from rickets from infancy until fourteen years of age in spite of treatment with vitamin D and supplements of calcium salts. The disorder was corrected by the daily administration of fish liver oil high in vitamin D. The dose started at the level of 122,000 U.S.P. units per day and was eventually reduced to about 50,000 units per day.

Studies of mineral metabolism showed that a positive calcium and phosporus balance could be maintained only when the intake of these elements was high. Otherwise both the calcium and phosphorus balances were negative. The changes in the balances corresponded to changes in the amounts of the minerals excreted in the feces. The urinary excretion of both calcium and phosporus remained practi-

cally unchanged with either high or low calcium diets.

Tracer experiments with radioactive phosphorus showed that phosphate was readily absorbed from the intestinal tract by the patient. The hypothesis is offered by the authors that the primary defect in this condition is not failure of absorption of the bone salts but rather in a failure of the calcifying mechanism.

The paper is illustrated with serial roentgenograms showing the rachitic changes in the bones at various intervals during the course of treatment.—*R. S. Bromer.*

FOLLIS, RICHARD H., JR., JACKSON, DEBORAH, ELIOT, MARTHA M., and PARK, E. A. Prevalence of rickets in children between two and fourteen years of age. *Am. J. Dis. Child.*, July, 1943, *66*, 1–11.

Two hundred and thirty children aged between two and fourteen years who died in the Harriet Lane Home from all causes were examined in consecutive autopsies for rickets. The total prevalence of rickets was found to be 46.5 per cent. The figures according to years indicated that the disease occurred with scarcely diminished frequency up to the fourteenth year. In 23 per cent of the total number studied the disease was classified as slight, in 18.7 per cent as moderate and in 4.8 per cent as advanced. In the white children the total prevalence was 43.6 per cent and in the Negro children 48.5 per cent. The prevalence of the disease in well developed degree was greater among Negro children.

No definite relationship between the occurrence of rickets and any particular disease could be established, with the possible exception of chronic lead poisoning. The prevalence of rickets among children dying of acute disease was greater than among those dying of chronic disease. The authors regard the significance of this as not clear. Disease may favor the development of rickets or, on the other hand, interfere with or actually block its development.

The greatest prevalence of rickets was in the winter months, December to February; the lowest, in the autumn months, September to November.

The fact is emphasized that the authors' studies dealt with a hospital population, not with the population at large. However, their study suggests strongly that rickets is a frequent occurrence in healthy-appearing children.

It was possible to recognize rickets by means of roentgen examination at most in 5 cases. They consider this fact not remarkable, since the characteristic roentgenographic signs are those which develop at the cartilage-shaft junction and changes there are apt to be confined to so narrow a stratum in children three or four years old. Because of the slower growth they do not show clearly. In still older children the changes at the cartilage-shaft junction may not develop at all, even though the shaft may be the seat of advanced involvement. With at most 5 exceptions, the rickets in the older children studied in this report could have given no outward signs of its presence.

The bones studied were the middle ribs.

The authors were totally unable to use Schmorl's classification of "beginning," "florid," "healing" and "healed" rickets, and they do not believe it is sound. They could not regularly differentiate between "beginning" rickets and slight rickets which had been present for a long time but had remained in a state of only slight development. They could also not distinguish between "healing" rickets in many cases and a very common form of the disease in which a healing process is operative all the time but never becomes sufficient to end the disease. They made no attempt to note those cases in which the rickets had entirely healed and only deformities were left.—*R. S. Bromer.*

KUHN, HAROLD H., and HEMPHILL, JAMES E. Baker's cyst: posterior herniation of the knee joint. *Radiology*, March, 1944, *42*, 237–240.

Baker described 10 cases of these synovial cysts and differentiated them from diseases of the knee joint. He at first believed they were the result of osteoarthritis. In 3 of his patients there was a true herniation through the posterior wall of the joint capsule.

These hernias usually develop gradually. With the patient upright and the knee extended the cystic swelling appears as a bulging mass on the medial aspect of the popliteal area distal to the popliteal skin creases. There is a soft, tender, non-fluctuating mass along the lateral aspect of the semimembranosus tendon. Differential diagnosis must be made from lipoma, hyperplastic bursitis, fibrosarcoma, angioma and arteriovenous aneurysm.

Diagnosis is made by injecting air into the joint and bandaging the lower third of the thigh so that the air is forced into any cyst that may exist. Roentgenograms with soft tissue exposure are then made. Two cases are described and roentgenograms given.

If these cysts are small they may be treated with a tight binder and a pressure pad over the the mass. If they are large enough to cause edema of the leg or interfere with the normal motion of the knee joint they should be removed surgically. If there is a pedicle it should be followed into the knee joint and its intra-articular part severed. The capsule is then closed completely which minimizes the possibility of recurrence.—*Audrey G. Morgan.*

Hauch, Paul P. Pneumoröntgenography of the knee joint. *Brit. J. Radiol.*, March, 1944, *17*, 70–74.

Strenuous training for military service has resulted in many injuries of the knee joint. Clinical examination can be usefully supplemented by roentgen examination of the joint after aspiration and the injection of 100 to 140 cc. of oxygen. An elastic bandage is applied tightly above the joint to force the oxygen into the lower compartments. The patient lies face downward with knees slightly flexed and films are made of each joint space in the anteroposterior position and in internal and external rotation. Forced adduction and abduction are applied in securing films of the internal and external spaces. Oxygen is used in preference to air as it is absorbed more quickly. No infection has followed the use of the method in any of the author's cases.

A series of 21 cases is reported with roentgenograms showing the normal appearance of the joint and various abnormal conditions. In 11 of the cases torn menisci were found. Other pathological conditions found were hypertrophied fat pads, loose bodies, Pellegrini-Steida's disease, discoid cartilage and postoperative absence of menisci.

Further development of this method will doubtless prove of great value in diagnosing cases of injury of the knee joint that cannot be diagnosed clinically. It will be even more accurate if there is close correlation of the clinical, operative and roentgen findings.—*Audrey G. Morgan.*

Marottoli, Oscar R. Sobre las fracturas de la apófisis externa del astrágalo. (Fractures of the external tuberosity of the astragalus.) *Rev. ortop. y traumatol.*, Oct., 1943, *13*, 107–117.

Fracture of the external tuberosity of the astragalus is extremely rare, only 6 cases having been published before this article was written. The publication of these 4 cases is justified by this rarity and by the fact that the lesion is often incorrectly diagnosed as sprain and the late results may lead to suits for damages.

The anatomy of the astragalus and its articulations is reviewed. The clinical signs of this fracture are inability to walk, marked edema of the ankle, ecchymotic infiltration of variable extent around the region of the external malleolus and an intensely painful point in front of and a little above the vertex of the external malleolus. A roentgenogram shows the tuberosity broken off at the level of the vertex of the external malleolus or only the most projecting part of the tuberosity may be detached. This form may be caused by strong traction on the ligaments. Generally there are no other bone lesions but in one of the author's cases a small fragment was broken off from the external malleolus and the internal malleolus was fractured, while in another there was incomplete fracture of the lower third of the tibia.

Four cases are described and illustrated with roentgenograms and photographs of operation. The fractures were caused by falling from a height and striking on the feet, or in 1 case by being struck by an automobile. In 2 of the cases a mistaken diagnosis of sprain had been made and the patients did not come to the author until nine and five months after the accident. In both these cases operation had to be performed and the detached part of the bone removed. In the other 2 cases the patients came for treatment immediately after the accident and consolidation was brought about by the application of a plaster cast and the use of Braun's apparatus.—*Audrey G. Morgan.*

Schearer, W. S. Ainhum. *Brit. J. Radiol.*, Jan., 1944, *17*, 25.

A case in an Indian soldier is described and illustrated with a roentgenogram. The fifth toes on both sides were greatly swollen and constricted at the base as if a tight ligature had been tied around each one. The shafts of the first phalanges of the fifth toes were narrowed

and the second and third phalanges of the fourth and fifth toes were fused. The cause of this disease is unknown. It occurs usually in dark races and the essential feature is constriction of the base of the small toe, and is almost always bilateral. The name comes from a native word meaning to saw or cut.—*Audrey G. Morgan.*

GENERAL

BAYLIN, GEORGE J. Body section roentgenography. *South. M. J.*, August, 1944, *37*, 418–424.

The author, in a well-arranged and excellently illustrated presentation, considers the application of body section roentgenography for the elucidation of lesions which are obscure or impossible of detection by conventional roentgenographic methods. He has found the procedure especially useful in demonstration of post-thoracoplasty cavity, bronchial tumors, bronchiectasis, the temporomandibular joint, tumors of the larynx and nasopharynx. He has been able to show sequestra in osteomyelitis of the femur when conventional methods failed because of density of bone, and he has obtained lateral roentgenograms of the thoracic spine free from objectionable shadows of superimposed parts. He concludes that the method has a definite and firmly established place in the roentgenologist's armamentarium.—*Angus K. Wilson.*

VALLS, JORGE E., and SCHAJOWICZ, FRITZ. Tuberculosis muscular hematógena. (Hematogenous muscle tuberculosis.) *Rev. ortop. y traumatol.*, Jan., 1944, *13*, 158–173.

Tuberculosis in muscle is generally secondary by direct propagation from bones, joints, tendons, etc. Its hematogenous transmission from foci at a distance is rare and a true primary tuberculosis of muscle can be brought about only by direct inoculation. Only a few cases of hematogenous tuberculosis have been described and those mostly in the German and Italian literature. This is probably because the disease is better known in those countries and it is doubtless often overlooked in countries where the picture is not known.

For this reason the authors give a detailed description of a case in a young woman of twenty-three who was admitted to the hospital with the picture of pulmonary tuberculosis. The right shoulder joint showed moderate muscle atrophy, limitation of movement and pain on movement of the arm. An abscess developed in the upper part of the arm and opened spontaneously. Later pain developed in the sacroiliac joint and a tumor of the anterior surface of the left arm. This tumor was operated on and proved to be a caseous mass in the muscle. Histopathological examination and animal inoculation proved it to be tuberculous. A photograph of the specimen and microphotographs of the histopathological findings are given.

Diagnosis of tuberculosis of muscle is difficult and is generally made only on operation. Treatment is surgical and cure can generally be brought about by removal of the foci even if they are multiple. Some authors recommend postoperative roentgen therapy. If the local condition of the focus and the patient's general condition do not permit of operation, evacuatory puncture, roentgen therapy and general treatment may be used. The prognosis of the solitary form is good; that of the generalized form depends on the condition of the original lesion and the patient's general health.—*Audrey G. Morgan.*

COLVIN, S, H., JR., GORE, IRA, and PETERS, MICHAEL. A case of histoplasmosis (Darling) with autopsy *Am. J. M. Sc.*, March, 1944, *207*, 378–385.

A study of the literature and a review of their own case leads the authors to conclude that histoplasmosis may be suspected when a patient presents continued fever, leukopenia, splenomegaly, hepatomegaly, anemia, lymphadenopathy, skin lesions and gastrointestinal ulceration. Clinically, however, the last three features were not present in this case, a colored male, aged twenty-three, whose occupation was a laborer and whose home was in Alabama. The diagnosis was not made before death and this has led the authors to point out several critical steps that may be taken in establishing a diagnosis. The more common diseases must be ruled out before considering the rarity. In the present case the clinical picture was confused by a roentgen diagnosis of miliary tuberculosis with which the finding of nine specimens of sputum negative for acid-fast organisms was not incompatible. It is thought that fungus was probably present in the sputa of this patient and if suspected could have been demonstrated by smear or culture. Again, more careful blood

studies, cultures, or bone marrow examination could have led to an ante mortem diagnosis as made in some of the previously reported cases. Biopsy of enlarged lymph nodes or of granulomatous skin, nasopharyngeal or gastrointestinal lesions constitutes the remainder of the diagnostic armamentarium.

The presence of anemia and leukopenia in histoplasmosis may be beautifully explained by the bone marrow findings in the present case as a quantitative reduction of the hematopoietic marrow by multiple granulomatous lesions which displace it. The presence of rather marked marrow hyperplasia between the granulomatous foci would speak against any marked toxic effect of the systemic infection.

Culturally the fungus grows as a yeast at 37°C., and produces mycelia with aerial hyphae at room temperature. Experimentally both forms are pathogenic but the mycelial form reverts back to the yeast form in tissues.—*James J. McCort.*

ROENTGEN AND RADIUM THERAPY

Ira I. Kaplan, One year observations of the treatment of cancer with avidin (egg white). *Am. J. M. Sc.*, June, 1944, *207*, 733–743.

This article is the report of a clinical test based on the hypothesis that cancer cells require biotin for their metabolic function and that egg white might seriously interfere with the vital function of malignant cells and thus bring about their destruction. This hypothesis was based on the observation of the close influence of biotin on cellular growth and that egg white or, more precisely, its constituent, avidin, possesses the ability to deprive the human system of biotin and thus possibly inhibit the influence of biotin on abnormal cell growth. In the experiments carried out each patient ate 36 to 42 egg whites per day with a general diet as free as possible from food rich in biotin along with a daily supplement of accessory vitamins and minerals. No untoward effects resulted from this diet and, as a whole, the general condition of the patient was markedly improved.

Eight case reports are given in some of which the malignancy showed a slight regression or the growth of the tumor was thought to be retarded. The cases selected were those that could readily be visually and clinically identified and the changes, if any, readily recognized. All cases were proved by pathologic study to be malignant.

The author states that as yet no definite cure of cancer has been effected by the use of egg white therapy as employed in this selected group of cases. He feels that as the diet given contained substantial quantities of milk which may have been a source of readily absorbable biotin this may have been one reason for the unfavorable results obtained. They were unable to produce a biotin deficiency in any of their patients. It is thought that an attempt should be made to improve the method of treatment with vitamins so as to balance the diet to such a degree that on the addition of avidin a biotin deficiency would be created.—*James J. McCort.*

Bean, William B., Spies, Tom D., and Vilter, Richard W. A note on irradiation sickness. *Am. J. M. Sc.*, July, 1944, *208*, 46–54.

This work was inspired by the discovery that the behavior of the urinary pigments and the codehydrogenases I and II following irradiation of the upper abdomen over the spleen resembled that in severely ill pellagra patients. Roentgen sickness is taken to include the nausea, vomiting, headache, cramps and diarrhea which complicate the course of therapeutic irradiation. It was planned to make a comprehensive investigation of the effect of a standard dose of radiation on normal well fed subjects; upon those given vitamin D deficient diet, with and without supplements of some of the vitamins in which the diet was deficient, and upon pellagrins and upon persons whose poor diet has caused ill health without other stigmata of a specific deficiency syndrome.

The radiation was given in all instances after an over-night fast (thirteen to sixteen hours after eating). An area over the spleen and upper abdomen was used. Four hundred roentgens were administered from a distance of 20 cm., using a Thoraeus filter, 200 kv., 20 ma., at the rate of 33 roentgens per minute.

The results of these studies were as follows: (1) normal persons consuming a good diet or on various vitamin B supplements had no ill effects except nausea in 1 white woman; (2) the sydrome of irradiation sickness in varying degrees of severity occurred in the rest of the patients, including the normal person who had subsisted on a vitamin B deficiency diet for six weeks; (3) roentgen therapy had no unpleasant

effects after nicotinic acid had been given during the last six weeks of a period of more than three months on the controlled diet but a week after the nicotinic acid supplement was discontinued the same amount of irradiation produced the characteristic reaction of roentgen sickness.

In all the cases studied there was a rough but by no means exact correlation between the severity of the reaction and the degree of vitamin depletion as gauged clinically.

Chemical studies showed there was no significant change in the blood level of biotin, pantothenic acid, riboflavin, or nicotinic acid. There was a fall in the cozymase and an increase of the glutathione level. The significance of this remains obscure.

It was concluded from these studies that the optimum time for vitamin therapy is before and not after the syndrome of irradiation sickness appears and that such therapy is essentially preventive in nature. The authors suggest that the basic disorder in roentgen sickness is a disturbance in respiratory enzyme system and point out the fact that since nutrition is often deranged in persons needing radiotherapy, the use of careful dietary and vitamin therapy is logical, if on empiric grounds alone.—*James J. McCort.*

LEDERMAN, M., CLARKSON, J. R., and MAYNEORD, W. V. Rectangular teleradium fields. *Brit. J. Radiol.*, April, 1944, *17*, 115–118.

Radium treatment is less readily manageable than roentgen treatment because of the fixed amount of radium and the fixed filtration and because few units are constructed so as to permit of variations in radium-skin distance or in the shape and size of fields. The authors chose certain rectangular fields to be used in the treatment of cancer of the head and neck. The applicators were made in a rectangular form and the dose contours measured by using a number of small condenser chambers exposed at the same time. The doses at given points in such fields can be measured by using the dose finder or the directional caliper. Illustrations of the apparatus and diagrams of its method of application are given.—*Audrey G. Morgan.*

GOIN, LOWELL S. Low-voltage contact irradiation therapy; further experience. *Radiology*, March, 1944, *42*, 241–245.

Five years ago the author discussed the basic principles of contact radiation therapy and outlined its uses. He now brings his experience with the method up to date. The essential conditions in the treatment are a short distance between the surface and the source of the radiation resulting in the absorption of a large amount of the energy in the first few centimeters of tissue. The depth dose is low. Consequently the treatment must be used for more or less superficial lesions and is not adapted for the treatment of deep-seated tumors.

He uses the Philips Metalix contact therapy unit, 50 kv., 2 ma.; the filtration varies from none at all to 2.5 mm. aluminum, 1.0 aluminum being used most commonly. The total anode surface distance is 22 mm., maximum 42 mm.

He discusses his use of this treatment in papillomas, keratoses, small keloids, small superficial hemangiomas, carcinoma of the bladder and epithelioma of the lip and skin. Very large doses can be given, much larger than in ordinary high voltage roentgen treatment. As a matter of fact the value of a roentgen in this method is probably different from that in other types of roentgen therapy so the doses are not comparable.—*Audrey G. Morgan.*

BUTLER, CARLOS. Cáncer de la mama; tratamiento y resultados. (Cancer of the breast; treatment and results.) *Radiología*, Jan.-Apr., 1944, *7*, 1–27.

Early treatment is particularly necessary in cancer of the breast because metastases appear early on account of the abundant lymphatic network of this organ. Therefore a campaign of education of women must be carried on so that they will go to a physician at once on the appearance of any tumor or any other suspicious sign. Such a campaign is being carried on and the number of cases coming for treatment in an early stage is increasing but still a great many cases come after the stage in which cure is possible has passed.

The author discusses 486 cases seen at the Radiological Institute in Montevideo. Of these 187 were in the first and second stages and 299 in the 3d, 4th and 5th stages; 374 had metastases and 112 did not; 420 cases were treated and 66 were beyond treatment. The best treatment is preoperative roentgen therapy, the technique of which is described in detail, followed after six to eight weeks by Halsted's operation with the electric bistoury, and this in turn after about two months by postoperative

irradiation. This treatment should be given in centers with a specially trained personnel and all the equipment necessary for carrying it out effectively.

The results are given in detail; 206 of the patients are dead. Of the patients with metastasis given combined roentgen-surgical treatment 53.3 per cent were cured for one to seven years, 33.3 per cent for more than three years and 13.3 per cent for more than five years. Of those without metastasis treated in this way 66.7 per cent were well for one to seven years, 50 per cent for more than three years and 33.3 per cent for more than five years.

If all cases could be brought to treatment in the first stage of the disease there is no doubt that these figures could be greatly improved.—*Audrey G. Morgan.*

PUENTE DUANY, N., CANIZARES, RAFAEL, and FONTS ABREU, ERNESTO. Cáncer de la mama; tratamiento y resultados lejanos. (Cancer of the breast; treatment and late results.) *Radiología*, Jan.-Apr., 1944, *7*, 28–37.

The authors discuss 602 cases of cancer of the breast seen from 1924 to 1937. Of these 100 have been followed up and have remained well for five years or more, 260 died and the rest were lost sight of. The results since 1930 have been much better than those before that time as they have had more adequate roentgen equipment and surgeons better trained in cancerology.

Various factors influence the prognosis, chief among which perhaps is early treatment; if cases could be brought to treatment in Stage I before there are axillary metastases the results could be improved greatly; correct diagnosis is of course essential and the treatment of the patient in an adequately equipped center. Treatment is more effective in older patients than in young ones. Unknown biological factors influence the degree of malignancy of different types of cancer. The scirrhous forms and also the colloidal forms develop slowly. Paget's disease and tumors originating in the excretory ducts show a comparatively favorable course.

The treatment used in these cases was surgery followed by roentgen therapy. Radical operation was performed in the majority of cases, simple mastectomy in some.

Until the cause of cancer of the breast is discovered the only way of improving the results of treatment is by early operation. The governments of all civilized countries should establish institutes of preventive medicine in all cities and all citizens more than forty years of age should be obliged to go for examination twice, or at least once a year, and special attention should be given to examination of the breasts and uterus in women. The best treatment of cases in Stage I should be studied more carefully and patients kept under observation for ten or fifteen years instead of the usual five years, for recurrences and metastases are often observed after that time.—*Audrey G. Morgan.*

CARVALHO, NELSON. Cancer do seio. Tratamento. Resultados. (Cancer of the breast; treatment; results.) *Radiología*, Jan.-Apr., 1944, *7*, 38–62.

The author insists on the value of a standardized classification of the different stages of cancer of the breast and the working out of the best plan of treatment for each stage. He defines the stages according to Steinthal's classification. Surgical treatment alone is effective in Stage I, but only about 10 per cent of the patients come for treatment during this stage. In this stage the cancer is limited to the mammary gland but this must be proved by microscopic examination. If the axillary glands have already become invaded when the patient first comes for examination, which occurs in 90 per cent of the cases, preoperative irradiation should be given to devitalize the cancer cells, followed by radical operation and postoperative irradiation. The results obtained by surgery alone can be improved by 60 per cent by using combined roentgen therapy and surgery. In advanced cases irradiation alone should be used. Though the results are only temporary they do prolong life and render the patient's life much more tolerable.

Removal of the ovaries cannot be recommended as a routine treatment but improvement is brought a out by sterilization in many cases with bone metastases. Each case should be studied carefully and thoroughly before sterilization is advised.

A discussion is given of 71 of the author's own cases which have been under observation for three years. In 68 per cent of these cases three year survival free of symptoms was brought about by combined surgical and roentgen treatment, while surgery alone applied to the same class of cases does not result in more than 25 per cent three year survivals.—*Audrey G. Morgan.*

GUZMAN, LEONARDO. Tratamiento de los cánceres del pecho y sus resultados. (Treatment of cancer of the breast and its results.) *Radiología*, Jan.-Apr., 1944, 7, 63–76.

The types of cancer of the breast are many and varied. Photomicrographs of a number of the forms are given, showing the marked differences in their cell structure. There are also many factors involved in their causation. Practically all of the endocrine glands have an action on the breast and in addition to that there is the factor of hereditary predisposition. It was formerly believed that cancer is at first a local disease that later becomes generalized through the blood or lymphatic circulation. It is now known to be a general disease that becomes localized in organs that are deficient or predisposed for some reason.

A very important point in prognosis is whether the axillary glands have become involved or not. But 15 per cent of glands that can be palpated are found to be free of cancer on microscopic examination and in the same percentage of cases there are microscopic changes in glands that could not be palpated before operation.

Other factors that may be involved in the causation of cancer of the breast are the effect of milk from a cancerous mother, retention of milk which becomes sour and brings about changes in the cells with which it comes in contact; toxic factors from liver disease or chronic constipation or from such diseases as tuberculosis and syphilis; all these factors may cause different types of tumor, depending on which of them act together at a given time on a breast that possibly already has an inherited susceptibility.

At present all these varied types of cancer are treated in the same way and that is probably one cause of the poor results obtained. It is to be hoped that further study will show what types of cancer can be treated by certain hormones or their antagonists, which may be cured by action on the pituitary gland or ovaries, which require surgery, which can be treated by antitoxins, etc. A brief review is given of the treatment at present advocated for different clinical types of cancer of the breast.—*Audrey G. Morgan.*

FRANGELLA, ALFONSO. Consideraciones sobre la roentgenirradiación del cáncer de la mama. (Roentgen irradiation of cancer of the breast.) *Radiología* Jan.-Apr. 1944, 7, 77–79.

Up to 1932 the author used the classical technique of Wintz in the treatment of cancer of the breast at the Radiological Institute of Montevideo but since that time he has used Holfelder's technique because it is better adapted to the anatomy of the breast and being given tangentially spares the lungs and pleura. Four fields are used, two 20×24 and the other two 15×20 or 10×15 cm. The two larger fields extend from the posterior axillary line to the sternal line and the smaller ones also encircle the breast but extend only from what he calls the mammary axillary line to the mammary sternal. The fields are irradiated in turn beginning with doses of 330 r and decreasing to 300, 270 and 240, with a total of 4,500 to 6,000 r depending on the size of the breast and the intensity of the biological reactions. In ulcerative or infectious cases, large doses cannot be given at first because they cause violent inflammatory reactions; a dose of 50 r is given at first, increasing to 100 and 150 r, and when the field is cleansed the larger tumor doses are given. In young women the preoperative irradiation is given in ten to twelve days, the total dose being not more than 3,500 to 4,000 r, in order to avoid very intense biological reactions; the surgeon can operate in three to four weeks.

Postoperative irradiation should not be used as a matter of routine but only in cases of great malignancy and ones in which the axillary glands are invaded. Postoperative irradiation has been called prophylactic but the author does not find that it is so. It is, however, very effective in irradiating involved glands which are more sensitive to irradiation than the original tumor of the breast.

Irradiation is the only effective method of treating generalized bone metastases. Large fields of 50 sq. cm. are used, with doses of about 30 r per day when localized fields are used and 15 to 20 r per day for generalized irradiation. These small doses have a very active effect on the blood picture and the platelet count may be used as a guide to dosage. The intense pain is quickly controlled and though the results are not permanent, the author has had patients who survived three and four years.—*Audrey G. Morgan.*

CAPRIO, GERARDO. Tratamiento radio-quirurgico del cáncer de la mama. (Radio-surgical treatment of cancer of the breast.) *Radiología*, Jan.-Apr., 1944, 7, 80–85.

In the treatment of cancer of the breast in patients from forty to sixty years of age, the author advocates surgery alone in cases that are in Stage I both clinically and pathologically. In cases that are in Stage I clinically but in Stage II pathologically—that is, with microscopic involvement of the axillary glands, surgery and prophylactic postoperative irradiation. In cases that are in Stage II clinically and pathologically, preoperative irradiation, radical mastectomy and postoperative irradiation. In cases in Stage III irradiation alone or in some cases simple mastectomy or electrocoagulation for cosmetic reasons.

In young women less than thirty-five years of age, the results of surgery alone have been discouraging. It is possible that they can be improved by radiotherapy. Teleroentgen therapy offers new possibilities. He does not advocate castration in young women because he thinks the bad psychic effects more than offset the advantages.

Radium treatment is complex and costly and roentgen therapy is to be preferred.—*Audrey G. Morgan.*

Terrizzano, Manuel F., and Terrizzano, Arturo J. M. La castración en el tratamiento radiante del neo del mama. (Castration in the radiation treatment of tumors of the breast.) *Radiología*, Jan.-Apr., 1944, *7*, 86–89.

The sex hormones tend to stimulate the growth of cancer cells due to the presence of the phenanthrene group which is also the cancer-producing element in cholesterol and tar. The authors therefore advocate sterilization in the treatment of cancer in young women. Preoperative irradiation of the cancer is given on alternate days with a dose of 400 r, giving a total of 1,600 r in eight days. On the intervening days the ovaries are irradiated from anterior and posterior fields with the same dosage. This is followed after about thirty to forty days by removal of the breast by Halsted's operation. Then after twenty-five to thirty days postoperative irradiation is given up to a total of 4,500 to 5,700 r in a month.

The authors have been using this method with good results in young women for the past five years. The clinical symptoms caused by the castration have not been severe and have been controlled by roentgen stimulation of the anterior hypophysis.—*Audrey G. Morgan.*

Cifarelli, Francisco P., and Pujadas, Amador A. Sobre los resultados de la roentgenterapia del cáncer mamario. (Results of roentgen treatment of cancer of the breast.) *Radiología*, Jan.-Apr., 1944, *7*, 90–92.

The authors use a Stabilovolt-Siemens apparatus, 180 kv., filter of 0.5 mm. copper and 1 mm. aluminum, distance 40 cm. In operated cases they use Wintz' technique, giving a dose of 350 r per day up to 1,750 r. In non-operated cases they use tangential irradiation, increasing the dose and the filter.

Among 151 cases they have treated, only 15, or 9.93 per cent, were in Group I; 106, or 70.2 per cent, were in Group II, and 30, or 19.8 per cent, in Group III. Roentgen therapy alone was used only in Group III. In Groups I and II surgery and postoperative roentgen therapy were used. They have only recently begun using preoperative irradiation and so do not consider it in their results.

All of the patients in Group I are living, some of them after seven and eight years. Among those of Group II 50 per cent are alive after four years, and half of these or more than five years. They have not been able to get reports on some of the cases of Group III and those from whom reports were received were in bad condition.

No changes were seen in the lungs in any of the cases resulting from irradiation. Recurrences were treated with roentgen therapy or surgery with good immediate results. They advocate roentgen castration in young patients. —*Audrey G. Morgan.*

Binnie, George G. Regression of tumours following treatment by stilboestrol and x-ray therapy, with notes on a case of breast tumour which regressed with stilboestrol alone. *Brit. J. Radiol.*, Feb., 1944, *17*, 42–45.

The author describes 3 cases in which malignant tumors of the breast were treated with a combination of stilbestrol and roentgen irradiation with good results and a fourth in which stilbestrol was used alone, also with marked improvement. This last case was not proved by biopsy to be malignant but he thinks it probable that it was a scirrshus of low malignancy.

The value of stilbestrol in carcinoma of the prostate has been proved and though his cases were all in the breast he believes it will prove equally effective in cancer in other regions and is now trying it. The majority of patients toler-

ate doses of 6 to 10 mg. stilbestrol daily over a long period without any ill effects except nausea and in some women menorrhagia. With continuation of the treatment, the menorrhagia tends to decrease. Some patients have a feeling of well-being in spite of the nausea and many show an increase in weight. The carcinogenic action of stilbestrol need not be considered as the patients already have advanced carcinoma. Radium has a very powerful carcinogenic action but no one hesitates to use it in the treatment of carcinoma. In all of the author's cases except the first one the treatment has extended over several months.

The number of cases is not large enough to justify definite conclusions but the author thinks it worth while to report them to stimulate further trial of the method.—*Audrey G. Morgan.*

McNATTIN, ROBERT F. Treatment of osteogenic sarcoma with preoperative roentgen radiation in large doses. *Radiology*, March, 1944, *42*, 246-248.

Early surgery has not proved effective in bone sarcoma. From a study of the literature and his own series of 8 cases, described here, the author concludes that the best treatment is preoperative irradiation followed by surgery as soon as the first signs of irradiation necrosis appear. He gives a long series of high voltage roentgen treatments using 200 kv (peak.), 0.5 mm. copper and 1.0 mm. aluminum filter, half-value layer 0.9 mm. copper, distance 60 to 70 cm. Multiple fields over the lesions are treated, one field daily with 250 to 300 r measured in air. Sixty to 140 treatments are given.

The delay of amputation due to this long series of treatments does not increase the probability of distant metastases. If a metastasis becomes manifest within six months after the beginning of treatment it already existed before treatment was begun. Biopsy is always contraindicated. Osteogenic sarcoma of bones other than those of the extremities should be treated more conservatively as severe irradiation necrosis may be dangerous.—*Audrey G. Morgan.*

LIVINGSTONE, J. L., BROCK, R. C., ROBERTS, FFRANGCON, DOBBIE, J. L., and HARNETT, W. L. Treatment of carcinoma of the lung; symposium. *Brit. S. Radiol.*, April, 1944, *17*, 101–109.

Livingstone emphasized the fact that in definite carcinoma of the lung the outlook is always fatal; but bronchial adenoma is frequently mistaken for carcinoma. He has one such case in which a fatal prognosis was given in 1932 and the patient is still alive and well. Bronchial carcinoma is quite common in men and so far irradiation has been palliative only. The only hope of improving the results is by early and accurate diagnosis. Tuberculosis must be excluded. He has found that cases with bronchial obstruction and infection do not do well under radiotherapy and he does not feel that the improvement brought about by intrabronchial radon compensates for the discomfort caused. He finds radiotherapy particularly useful in the following conditions: In a mediastinal mass which may be Hodgkin's disease or oat-celled carcinoma a rapid decrease in size may be diagnostic; in peripheral tumors, especially when there is great pain; in localized secondary growths in the chest; in postoperative treatment after removal of carcinoma of other organs.

Brock says that the only hope of successful treatment for these patients is surgery. The best method is removal of the whole lung and its lymphatic glands by dissection. Lobectomy is incomplete but may be used in elderly patients in whom total removal of the lung would be too great a risk. He believes the latter operation can be performed in about 10 per cent of patients with bronchial carcinoma. He has performed the operation in 32 cases and 9 of the patients died of the operation, a mortality of 28 per cent. This includes his early cases in which he was experimenting more or less and also includes patients over sixty years of age in whom the operation is particularly dangerous. In reasonably favorable cases the mortality should not be more than 15 per cent. Among the 23 patients who survived the operation there was recurrence in eight. The length of survival in other cases has been up to four and a half years. Graham reports a patient who is alive and working ten years after operation. These patients can do anything but very heavy work after operation.

A very small tumor may cause a large opacity in the roentgenogram, which makes it difficult to determine dosage in roentgen therapy.

Roberts disagreed with Brock with reference to the usefulness of surgery and the uselessness of radiotherapy. He points out that Brock's own reported mortality was high and says

there is no justification for Brock's statement that radiotherapy hastens death. He takes exception to Brock's pointing out the conditions under which radiotherapy should be used and says that that is the province of the radiotherapist and not the surgeon. The latter has only to decide whether he shall operate or not. He considers radiotherapy from the point of view of relief of symptoms, prolongation of life and possibility of cure. Even in advanced cases there may be considerable relief of symptoms. It is hard to estimate the degree of prolongation of life as large series of cases must be considered and each physician or clinic has only a small number. In considering the possibility of cure the characteristics of bronchial carcinoma must be known. A very small tumor may cause a very great disturbance of general health and there is a marked tendency to early dissemination by the blood stream. He formerly used large fields but now uses a double ring of small fields, four in the inner ring and eight in the outer, with a general design somewhat like that of a Tudor rose. With 1,200 r given to each field the total dose may be 28,800 r or even larger. The largest possible dose should be given with the least possible general disturbance. There are no satisfactory figures for depth doses to the lungs. He is now working on the problem. He does not expect any substantial improvement in results from either surgery or irradiation. Any improvement must come from fundamental research and the results will probably be long in coming.

Dobbie reported 170 cases treated by irradiation at the Christie Hospital and Holt Radium Institute from 1935 to 1942. These patients were younger than the usual cancer patients, 9 per cent of them being between thirty and forty. Pain and hemoptysis are the most constant symptoms. He recommends greater use of tomography in diagnosis. He has found bronchoscopy disappointing. Seventy per cent of these tumors were anaplastic. These tumors are unsuitable for surgery. Palliative treatment was given in 111 cases, necessarily with large fields. Twenty-six per cent of these patients lived for more than six months, in some cases with striking symptomatic relief. There was some degree of relief in 40 per cent of the cases. The radical treatment is based on the assumption that many of these tumors are quite small and a large dose is given to a small volume of lung tissue around the tumor. A dose of 6,000 r in five weeks or an equivalent dose at shorter intervals is prescribed, but too little is known of depth dosage in lung tissue and when a more thorough knowledge of this subject is available the results will probably be better. The author has not found these large doses harmful to the patients. Fifty-nine patients were treated by this method; 11 are alive and 48 dead. Among the dead patients 21 per cent survived for a year or more.

Harnett, who is Medical Secretary to the Clinical Cancer Research Committee of the British Empire Cancer Campaign, reports that out of 15,200 cases of cancer registered in the seventeen months up to September, 1939, there were 1,023 cases of primary bronchial carcinoma. The ratio of males to females was 4.6 to 1, and the average age was 55.9 years for males and 57.7 for females. The cases of bronchial carcinoma constituted 11.5 per cent of all cancer cases in males and 2.3 per cent of those in females. Fifty-nine per cent of these cases were so far advanced when first seen that they were only suitable for palliative medical treatment and 12 per cent were given palliative surgical treatment. Exploration of the chest was made in 5 per cent of the cases but only 1.5 per cent were found suitable for pneumonectomy; 20 per cent were treated with deep roentgen therapy while 1.4 per cent and 2.3 per cent were given intrabronchial radon and interstitial radon treatment respectively. The average duration of the disease in the whole series counting from the time when the first symptoms were noticed to death was 10.2 ± 0.3 months. Taking only the 294 cases in which the disease was judged to be still local the average duration of life was 13.3 months in males and 14.1 months in females. A table is given showing the survival rates in treated and untreated patients.—*Audrey G. Morgan.*

DOUGLAS, S. J. Cancer of the lip. *Brit. J. Radiol.*, June, 1944, *17*, 185–189.

The author reports 71 consecutive cases of cancer of the lip treated at St. Anne's Hospital, Dublin, during the year 1939. The incidence of cancer of the lip is high in men engaged in farming and other outdoor occupations, probably because of the frequency of oral sepsis, prevalence of pipe smoking and exposure to wind and sun. The average duration of symptoms before these patients came for treatment was eight months, and in some cases as long as five or six years. It is important that the public

be instructed to come for examination at once when any lump, scaly patch or ulcer appears on the lip. Also that medical students be taught the early appearance of cancer of the lip. Many physicians believe that cancer of the lip is shown only by a large fungating ulcer. If the disease is allowed to reach this stage treatment is almost hopeless.

Of these cases 16 were treated by radium implantation and 46 by contact roentgen therapy. Of those treated by radium 6 were alive and free of disease when last seen. These cases are particularly adapted for contact roentgen therapy. A total surface dose of 8,000 r is given in ten daily doses of 800 r each, treatment being given five days per week. Details of the technique are given. Of these 46 cases 37 are alive and well three years after treatment.

The best treatment for gland metastases is block dissection followed by treatment of the primary lesion. Among the whole 34 cases that showed adenopathy in this group 18, or 53 per cent, are alive and free from disease.—*Audrey G. Morgan.*

KAPLAN, IRA I. Hemangioma of the elbow successfully treated with radium at an early age. *Am. J. Dis. Child.*, May, 1943, *65*, 785–787.

Kaplan reports the case of a patient with a hemangioma of the elbow which was treated at an early age, ten weeks. The treatments were given at intervals for a period of eleven months and the patient was followed for a period of nine years. At the time of her last observation the lesion was completely healed and there was no impairment of articular function. There was also no evidence of involvement of bone nor of impairment of epiphyseal growth or of any discrepancy in length of the bones of the treated arm. The radium had been applied directly over the elbow joint, opposite the epiphysis where effects of radium application on the bone are most likely to be noted. Kaplan concludes that fear of adversely affecting growing bones in children with radium therapy are fallacious if irradiation is properly and expertly administered.—*R. S. Bromer.*

BEILIN, DAVID S. Clinical features, diagnosis, and treatment of carcinoma of the colon and rectum. *Radiology*, June, 1944, *42*, 539–544.

A series of 117 cases of carcinoma of the colon and rectum is discussed, the oldest patient being eighty-four years of age and the youngest thirty-two; average sixty years. There were 60 females and 57 males.

Of these tumors 9 per cent were in the cecum, 7 per cent in the ascending colon, 2.4 per cent in the hepatic flexure, 11 per cent in the transverse colon, 8.5 per cent in the splenic flexure, 10 per cent in the descending colon, 22 per cent in the sigmoid, 22 per cent in the rectosigmoid, and 5.9 per cent in the rectum. These figures show that almost half of the cancers of the large bowel are in the pelvic colon.

The most prominent symptom of these cancers of the large bowel is pain, which may or may not be colicky in nature, with diarrhea or constipation. There is often anemia, weakness, loss of weight and a palpable tumor. The average duration of symptoms when the patient came for treatment was about eight months.

There are no pathognomonic symptoms of this condition but the majority of cancers of the rectum and sigmoid can be diagnosed by careful manual and proctosigmoidoscopic examination and the greater part of those proximal to the rectosigmoid can be diagnosed by roentgen examination and the localization determined.

The preferred operation in cases of cancer of the rectum and rectosigmoid is abdominoperineal resection; in those higher up the operations performed were Mikulicz' resection, short-circuit operation, palliative cecostomy or colostomy, or resection with permanent colostomy. The results depend partly on the extent of the disease and partly on the skill of the surgeon.—*Audrey G. Morgan.*

MELBIN, M., and STENSTROM, K. WILHELM. Results of treatment of 173 cases of carcinoma of the rectum. *Radiology*, June, 1944, *42*, 545–549.

Eight per cent of all cancers are in the large bowel and half of these are in the rectum.

The authors discuss 173 cases, 69 of which were treated surgically and with irradiation, while 104 were treated by irradiation without operation or with only a colostomy. Five of the surgical group were at first thought to be inoperable but they improved so much under irradiation that operation could be performed. One of these patients in whom the tumor had infiltrated the bladder lived twelve years and died of pernicious anemia without recurrence. In recent years Miles' one stage combined abdominoperineal resection has been the opera-

tion used. Details of the roentgen therapy, which has varied greatly in the course of years, are given. Local radium therapy is generally given after the external roentgen irradiation is completed.

Among the patients treated surgically the five year survival rate was 34 per cent, while among those without surgery or merely a colostomy it was 5 per cent.

Adequate irradiation of cancer of the colon is not merely palliative. The mean life expectancy of untreated cancer of the rectum from the beginning of symptoms to death has been reported as fourteen months. The patients in this series treated by irradiation without operation showed an average length of life of twenty-one months. In a small number of cases cures are brought about by irradiation alone.—*Audrey G. Morgan.*

Borak, J. Theories on the effectiveness of roentgen therapy in inflammatory conditions. *Radiology*, March, 1944, *42*, 249–254.

Since 1926 it has been known that roentgen therapy has a favorable effect on inflammatory conditions even in the most acute stage if very small amounts are given. A dose of moderately filtered rays of from 50 to 150 r has proved very effective in many inflammatory conditions caused by streptococci and staphylococci, gonococci, pneumococci and meningococci. The small dose and the rapidity of its action are the most striking features of this treatment.

This effect has been attributed to a direct bactericidal action of the rays, to an action on the blood, on the exudate and on the blood vessels. Arguments are presented showing that it is not due to direct bactericidal action, or to action on the blood or exudate but to action on the blood vessels. Irradiation does not cause an increase of the antibodies in the blood of the patient but leads to a concentration of the antibodies in a definite area and for a definite time.

It has the effect of both heat and cold but to a milder degree. Like heat it causes a dilatation of the capillaries but like cold it causes a narrowing of the arteries. Like heat it causes retrogression due to resorption through the lymphatics or perforation through the skin from abscess formation. Like cold it lessens the hyperemia and exudation. This combination of effects shortens the inflammatory process more quickly and to a greater degree than can be accomplished by any other conservative method of treatment.—*Audrey G. Morgan.*

Pool, H. H. Roentgen therapy with low dosage in suppurative infections. *Radiology*, March, 1944, *42*, 255–257.

The usual dose of roentgen rays in the treatment of infections has been 100 r. As the chief action is on the leukocytes in the inflamed area the author concluded that a lower dosage might be effective in cases in which the inflammation did not recede promptly under this dosage. He therefore reduced his dosage successively to 80 r, 65 r, 50, 35 and finally 25 r. Increasingly better results were obtained as the dosage reached 50 r and below. For the past year he has used 25 r in most cases. Sulfa drugs can be used in association with these low doses without injuring the skin as they cannot with higher dosages.

A table is given showing the treatment and results in 59 cases of various inflammations including axillary abscesses, abscesses of the jaw and neck, mastoiditis, carbuncles, cellulitis, erysipeloid infection, otitis media, infected traumatic wounds, infected operative wounds, abscess of the breast, styes, furunculosis of the ear canal, peritonsillar abscess, acute sinusitis and unresolved pneumonia, The author does not hold that 25 r is the optimum dosage in every case but he thinks that the dose should not be more than 50 r and that 25 r is sufficient in 90 per cent of the cases. He has had excellent results in unresolved pneumonia, in which the treatment should be as in other infections, allowing only for depth. He has had only 1 case of infected traumatic wound but he believes all such cases could be more safely handled with prompter healing if short courses of roentgen treatment were given. This would result in an enormous saving of days for productive effort and much suffering would be prevented. Very little surgery is needed in carbuncles and abscesses with this method of treatment. Nearly 85 per cent drained spontaneously, requiring no incision. Two of the patients with carbuncles were diabetic. The response to treatment was as good as in non-diabetic cases.—*Audrey G. Morgan.*

Freireich, Kal. Radiation therapy for obstructing tuberculous hilar lymph nodes. *Am. Rev. Tuberc.*, Jan., 1944, *49*, 31–37.

Enlargement of the regional tracheobronchial and bronchopulmonary lymph nodes is an essential component of primary complex pulmon-

ary tuberculosis. Generally, such nodes shrink, fibrose, and calcify without producing symptoms. However, not infrequently the hilar nodes become extremely large, compress the tracheobronchial tree, and culminate in obstructive emphysema, atelectasis, and bronchiectasis. Furthermore, a caseous node may invade the bronchial wall thereby producing an ulcerative bronchitis or may rupture into the bronchial lumen, resulting in a massive bronchiogenic tuberculous spread.

Jones, Rafferty and Willis refer to atelectasis produced by tuberculous lymph node pressure as "epituberculosis." They have seen 85 such cases over a five year period. Forty-two of their cases were bronchoscoped, and 17 demonstrated narrowing of the bronchial lumen by external pressure. Ten of the 42 cases died—attesting to the serious prognosis of the condition. Myerson bronchoscoped 29 tuberculous children and 13 showed major bronchial lesions —7 of which were due to lymph node pressure. In his adult group, approximately 1 per cent showed bronchial tuberculous lesions attributable to lymph node pressure.

The author was unable to find a report of a single case of hilar tuberculous lymphadenitis treated by roentgen therapy. He reports the case of a seventeen year old colored girl who entered the hospital in July, 1941, with roentgen evidence of a right pleural effusion and enlargement of the left hilar nodes. A roentgenogram in February, 1942, demonstrated definite narrowing of the left main bronchus just distal to the tracheal bifurcation. Bronchoscopic examination performed in July, 1942, demonstrated a marked widening of the carina; the left main bronchus was narrowed to a slit; and the lumen of the right main bronchus was compressed from without. Despite bed rest, dyspnea increased sufficiently to cause respiratory embarrassment and wheezing became increasingly troublesome. Roentgen therapy was begun in October, 1942. Six treatments of 112 r (200 kv., 0.5 mm. copper filter) were delivered alternately at weekly intervals to the anterior and posterior mediastinum—a total of 336 r being delivered to the anterior and a similar dose to the posterior mediastinum for a total dose of 672 r.

The result was dramatic—after the first treatment, the wheezing diminished and following the third treatment, the dyspnea and wheezing disappeared completely. Roentgenographic and bronchoscopic studies confirmed the clinical impression of marked decrease in bronchial compression. No adverse affects on the pulmonary tuberculosis were demonstrable during the eight months following treatment.

Radiation therapy would appear to be a safe form of treatment to be tried in certain cases of marked tuberculous hilar lymph node enlargement which threatens to produce severe bronchial compression. This therapy should always be used in consultation with a skilled radiation therapist.—*John R. Hannan.*

MISCELLANEOUS

McCAW, W. W. Training of x-ray technicians at the School for Medical Department Enlisted Technicians. *Radiology*, April, 1944, *42*, 384–388.

At the outbreak of the present war there was only one school in the Army for training technicians, that at the Army Medical Center, Washington, D. C. There are now schools at nine Army General Hospitals and hundreds of roentgen-ray technicians have already been trained. The author, working at the Fitzsimons General Hospital in Denver has had an opportunity to observe the results of this training. The course for roentgen-ray technicians now extends over a period of three months, during which time the student is given 504 hours of technical instruction; in addition he is given an hour and a half a day of military training. During the first month he is familiarized with the electrophysical principles involved in the production of roentgen rays, the nature and physical properties of the roentgen-ray beam and the way in which roentgen rays are made use of in roentgenography. The second month he takes up the technique of roentgenography and is instructed in radiography, film criticism osteology and laboratory work. The last month includes a brief introduction to roentgen therapy; lectures are also given on the ethics of roentgen-ray technicians.

Most gratifying reports have been received from radiologists in Army hospitals on the results of this training and the author recommends the establishment of similar schools in civilian practice so that the training program for roentgen-ray technicians may be more or less standardized throughout the country.—*Audrey G. Morgan.*

Rogers, G. L. Instantaneous stereography. *Brit. J. Radiol.*, April, 1944, *17*, 122–125.

Instantaneous stereography is useful in studying the heart, the viscera, arteriograms, phlebograms and possibly the lungs; also in the exact location of radium needle implantations.

The method described here is based on the parallax stereoscope of St. Ives which has been modified for roentgenologic work. The method is promising and worth further development. A figure is given showing the general details which are applicable to both taking and viewing. In taking, the two apices represent the two foci of a bifocal tube or the anodes of two portable tubes run together. Roentgen rays diverge from these points, traverse the object space and are cut up by a grid into thin parallel strips. The apparatus is so arranged that the rays fall on the film in alternate strips, one coming from one anode and the next from the other. In this way the two stereoscopic views are cut up into interdigitating strips. This involves a certain loss of image but in practice the loss is not serious. In viewing, the composite film is placed behind a viewing grid—which can be a photographic replica of the taking grid—and the eyes are placed in a position geometrically similar to the position of the taking anodes. Each eye then sees its appropriate image through the grid. The advantage of this method of viewing over the standard method is explained. Certain avoidable errors in the standard procedure are discussed.—*Audrey G. Morgan.*

Morgan, Russell H. Reciprocity law failure in x-ray films. *Radiology*, May, 1944, *42*, 471–479.

The reciprocity law which is one of the fundamental rules of photography and roentgenography states that the quality of a series of roentgenograms will be uniformly constant if the exposure time with which they are made varies reciprocally with the intensities of the exposing radiation. It implies that, other things being equal, a roentgenogram exposed for 1.0 second with a tube-current of 100 milliamperes will be identical with one exposed for 10 seconds with a tube-current of 10 milliamperes. The law is based on the assumption that the density or blackening of a photographic film is dependent only on the exposure or quantity of radiant energy which the film absorbs and is independent of the rate at which the energy is applied, that is, it is independent of the intensity of the exposing radiation. But it has been found that this is not true, but that photographic quality is dependent not merely on the quantity of radiant energy absorbed by the film but also on the intensity of the exposing radiation. The chief significance of reciprocity law failure is its effect on the sensitivity or speed of a photographic emulsion.

The methods of studying reciprocity law failure, its significance and the theoretical considerations on which it is based are discussed and graphs given illustrating the findings in regard to reciprocity law failure in four brands of roentgen films.—*Audrey G. Morgan.*

Ellis, F., and Miller, H. The use of wedge filters in deep x-ray therapy. *Brit. J. Radiol.*, March, 1944, *17*, 90–94.

In the treatment of deep tumors by roentgen rays it is hard to irradiate the tumor uniformly without injuring the normal tissues beyond it. For this purpose the authors introduce a wedge-shaped absorber into the beam. It is arranged so that the thickness of the absorber increases gradually from one side of a rectangular field to the opposite side so that in any plane at right angles to the central ray the dose is reduced progressively in passing across the field.

Two methods of utilizing the wedges may be used. In the first, two wedge fields are combined at right angles, that is along the adjacent edges of a square, in such a way that the thick edges of the wedges lie along a common line. The second method is used when the distance between two roughly parallel surfaces of the body is relatively small, as in treating the larynx or axilla. In these cases the use of two parallel opposed wedge fields and a direct field at right angles to them gives a very uniform dose distribution. Wooden wedges are very satisfactory for this purpose as the absorption of radiation in wood is very similar to that in tissue. Isodose curves are given for these two methods of use. Descriptions and photographs are given of different types of wedges used.—*Audrey G. Morgan.*

Spencer, R. R. The place of the National Cancer Institute in the cancer problem. *Radiology*, May, 1944, *42*, 493–498.

Thirty years ago the American Society for

the Control of Cancer was launched with the object of educating the public and physicians to understand the importance of early diagnosis and expert treatment of cancer. The activities of this Society resulted in the passage of the National Cancer Institute Act in 1937. The National Cancer Institute, established under this act, provides training in diagnosis and treatment of cancer for a group of young physicians particularly interested in this subject. On completion of their training they are capable of setting up and directing tumor clinics to conform to the standards of the American College of Surgeons.

The National Cancer Institute has purchased 9.3 gm. of radium, about 8 gm. of which has been loaned to hospitals throughout the country for the treatment of cancer patients. No charge is made for the use of this radium and preference must be given to indigent patients. The Cancer Institute cooperates with state health departments in the prevention, control and eradication of cancer. The states endeavor to provide for free or part-pay aid in the diagnosis and treatment of cancer patients, free tissue diagnosis, lay and professional diagnosis and statistical and epidemiologic research, including a system of follow-up of cancer cases. The Institute also prepares films and posters for public education, emphasizing the curability of *early* cancer. In the past five years the Institute has recommended that over $400,000 be paid to various institutions for research in various phases of the cancer problem, particular emphasis being placed on cancer of the stomach which causes about 25 per cent of all deaths from cancer.

Since 1939 when the National Cancer Institute building was completed the most significant research work has been in the field of carcinogenesis. Some of the details of this work are described and the suggestion is made that cancer may be caused by a process of adjustment of cells to some unusual environmental condition. Work is just beginning on cancer treatment and the development of reliable tests for the early diagnosis of the disease. Other studies are being made on the metabolism of normal and cancer tissue, the part played in the problem by vitamins and other nutritional factors and by hormones and enzymes. Emphasis is placed on the fact that cancer is a national medico-socio-economic health problem and that it can no longer be left to the individual worker but that the work must be done systematically by organized research groups.—*Audrey G. Morgan.*

PATERSON, EDITH. The time-intensity factor in x-ray irradiation. Part I. The influence of the overall time. *Brit. J. Radiol.*, Jan., 1944, *17*, 26–30.

Experiments were made on chick fibroblasts to determine whether the effect of irradiation is influenced by changes in the overall time of irradiation, that is the time from the beginning of the first exposure to the end of the last. During these experiments the total dose and the dosage rate, that is the number of roentgens delivered per minute, were kept constant. Tables are given showing the details of the results. It was found that when the overall time was prolonged the irradiation was more effective, as shown by the fact that both survival rate and survival time were lowered as compared with short-term irradiation. There was also a reduced variation in the time of death so that the survival times were more homogeneous. Nor did the cells show recovery as they did after short time irradiation. The effect was also influenced by the number of sessions into which the dose was split. The effect was greater when the total dose was split into eleven sessions than when it was given in three or four.

These experimental facts do not necessarily hold good in clinical therapy but if they are found to apply there also it would mean that long-term irradiation with suitable splitting produces better effects and shows fewer recurrences than short-term irradiation.—*Audrey G. Morgan.*